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# Minnesota Medicine

Journal of the Minnesota State Medical Association, Southern Minnesota Medical Association, Northern Minnesota Medical Association, Minnesota Academy of Medicine and Minneapolis Surgical Society

Volume 37

August, 1954

Number 8

## Symposium on Fluid and Electrolyte Balance

One hundred and thirty-six years have passed since Claude Bernard referred to the composition of fluids surrounding cells as the "milieux interieur." Since that time there has been a progressive accumulation of knowledge of the physiology of fluid and electrolyte balance in man and experimental animals.

The past ten years have witnessed a remarkable growth in the clinical usefulness of basic fluid and electrolyte physiology, so that a working knowledge of new terms and techniques of water and electrolyte balance have become essential in the care of many medical and surgical diseases. The "milli-equivalent doctor" and the "get-em-well doctor" have become one and the same.

It is the purpose of this "Symposium" to pre-

sent in a useful way the fundamental physiology of body fluid and electrolytes with an approach to the application of recent knowledge in the everyday care of patients. This series of articles, including the basic physiology, pediatric, medical and surgical facets of fluid and electrolyte balance, has been prepared through invitation by Dr. Edward B. Flink, associate professor of medicine,\* Dr. Richard Raile, instructor in pediatrics, Dr. Howard Worthen, research fellow in pediatrics, and Dr. Bernard Zimmermann, assistant professor of surgery, University of Minnesota.

S. W. A.

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### FLUID AND ELECTROLYTE BALANCE

#### Part I: Basic Considerations

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SINCE it has become apparent that a symposium on electrolyte and fluid problems might be of value at this time, the authors have planned to review the most important general principles and the most pressing problems involved in clinical fluid and electrolyte disturbances. It is our aim to make this series of articles useful practical guides to diagnosis and therapy.

#### Balance

To start with, it is important to define some terms and to explain the arithmetic of this subject. The idea of balance or equilibrium in its basic principles is as simple as a bank balance. Any element or substance for which adequate analyses are available and which enter into metabolism can be measured in terms of balance. A negative balance means a deficit of the substance

and a positive balance means storage of an excess. When intake equals output, then balance or equilibrium exists. One of the most difficult problems, however, is to ascertain that a patient has a deficit or an excess when he is first seen and intake and output data are not available.

#### Dehydration

Dehydration is strictly defined as a deficiency in water. Simple water deprivation, however, is infrequent, it being much more commonly accompanied by a concomitant loss of electrolytes.

#### Acidosis and Alkalosis

Acidosis and alkalosis are terms used to indicate deviations of the acid-base equilibrium from normal. PH is a convenient logarithmic representation of the reciprocal of the hydrogen ion

## FLUID AND ELECTROLYTE BALANCE—FLINK AND ZIMMERMANN

**TABLE I. COMMON IONS IN BODY FLUIDS**  
(Atomic and molecular weights  
are recorded to the nearest gram).

	Atomic Weight	Equivalent Weights
Simple Ions		
Sodium ( $\text{Na}^+$ )	23 Gm	23 Gm
Potassium ( $\text{K}^+$ )	39 Gm	39 Gm
Calcium ( $\text{Ca}^{++}$ )	40 Gm	20 Gm
Magnesium ( $\text{Mg}^{++}$ )	24 Gm	12 Gm
Chloride ( $\text{Cl}^-$ )	35 Gm	35 Gm
Complex Ions		
*Phosphorus ( $\text{HPO}_4^{2-}$ )	31 Gm	31/1.8†
*Sulfur ( $\text{SO}_4^{2-}$ )	32 Gm	16
**Carbon Dioxide ( $\text{CO}_2 + \text{HCO}_3^-$ )	22.26 liters	22.26 liters

\*Determined in terms of mg. of sulfur or phosphorus usually.

\*\*Note that carbon dioxide is measured as a gas.

†Factor takes into account small amount of monovalent ( $\text{H}_2\text{PO}_4^-$ ) at pH of serum.

**TABLE II. MOLECULAR WEIGHT OF SALTS  
COMMONLY USED IN THERAPY**

Sodium chloride	58
Potassium chloride	74
Ammonium chloride	53
Sodium bicarbonate	84
Sodium lactate	112

concentration. The body tries to maintain pH in a very narrow range (7.35-7.42). In order to elucidate acid-base problems, pH determinations have been invaluable and are very helpful clinically if available, but can be usually dispensed with in most ordinary clinical cases. The details of acid-base regulation will be discussed below.

### Milliequivalents

Electrolytes (particularly sodium, chloride, carbon dioxide and potassium) are best reported and thought of in terms of milliequivalents per liter rather than by any other units. This is as reasonable as counting assets in terms of dollars and cents instead of pounds of tin, copper, salt and bread. The sum of ions with a positive charge (cations) must equal the sum of ions with a negative charge (anions). Since equivalents are an expression of the number of ions, the same equality holds when values are expressed in terms of equivalents or milliequivalents. It does not, of course, apply to other units such as milligrams.

An equivalent weight of an element is the atomic weight divided by the valence of the element. A milliequivalent weight is 1/1000 of an equivalent weight. A milligram being 1/1000 of a gram, milligrams per liter can be converted to milliequivalents per liter by merely dividing the value in milligrams by the equivalent weight. Since a molecular or equivalent weight of carbon

**TABLE III. SAMPLE CALCULATIONS OF  
ELECTROLYTE CONCENTRATIONS**

	Mg/100 cc serum	Mg/liter	mEq/liter
Sodium ( $\text{Na}^+$ ) Chloride (as $\text{NaCl}^*$ )	325 580	$\times 10 = 3250$ $\times 10 = 5800$	3250/23 = 141 5800/58 = 100
Protein	7.0		7 x 2.43** = 17
$\text{CO}_2$	55 cc	$\times 10 = 550$ ee	550/22.2 = 24.8

**TABLE IV. NORMAL VALUES OF ELECTROLYTES  
IN SERUM (mEq/1)**

Basic ions (cations)	Acid ions (anions)	Sum equals 130
$\text{Na}^+$ 138-145	$\text{Cl}^-$ 100-106	
$\text{K}^+$ 4-5.6	$\text{CO}_2$ 23-28	
$\text{Ca}^{++}$ 4.5-5.5	$\text{PO}_4$ 1.7-2.3	
$\text{Mg}^{++}$ 1.5-2.1	Protein 14-17	
	$\text{SO}_4^{2-}$ 5-1.0	sum of these equals about 25
Average 155 mEq/1.	Organic Acids 5-7	
	155 1 mEq/1.	

\*Most laboratories report chlorides in terms of milligrams of molecular sodium chloride per 100 cc rather than as mg. of chloride alone. \*\*2.43 is a derived factor for this conversion.

dioxide ( $\text{CO}_2$ ) occupies 22.26 liters, the factor 2.23 is used to convert volumes per cent to mEq./1.

Osmotic pressure means the pressure which a dissolved substance (solute) exerts when confined by a membrane which it cannot penetrate. An osmolar solution contains one molecular weight of a solute. Ionized solutes exert an osmotic effect equivalent to the number of ions in a molecule. A milliosmolar solution refers to 1/1000 of an osmolar solution.

Tables I and II record the atomic weight, equivalent weights and molecular weights of the elements and compounds which are of clinical importance.

In order to illustrate methods of conversion, sample calculations for hypothetical values of  $\text{Na}^+$ ,  $\text{Cl}^-$ , Protein and  $\text{CO}_2$  are given in Table III.

Table IV gives the normal range of values for serum electrolytes.

Ions other than  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$  and  $\text{HCO}_3^-$  which are present in small concentration are frequently recorded in terms of milligrams or grams. For the sake of uniformity, however, it is better to report all of them as milliequivalents. As is implied in Table IV, the sum of the two main anions  $\text{Cl}^-$  and  $\text{CO}_3^{2-}$  is a clinically useful figure. Sodium is the main cation and magnesium and calcium vary within such a small range that their contribution to osmolarity is relatively fixed. Similarly

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the small range within which potassium varies is of little consequence from the osmolar standpoint, though, as will be shown later, it has highly

The advantages of recording chemical values in terms of milliequivalents are further illustrated by the following samples:

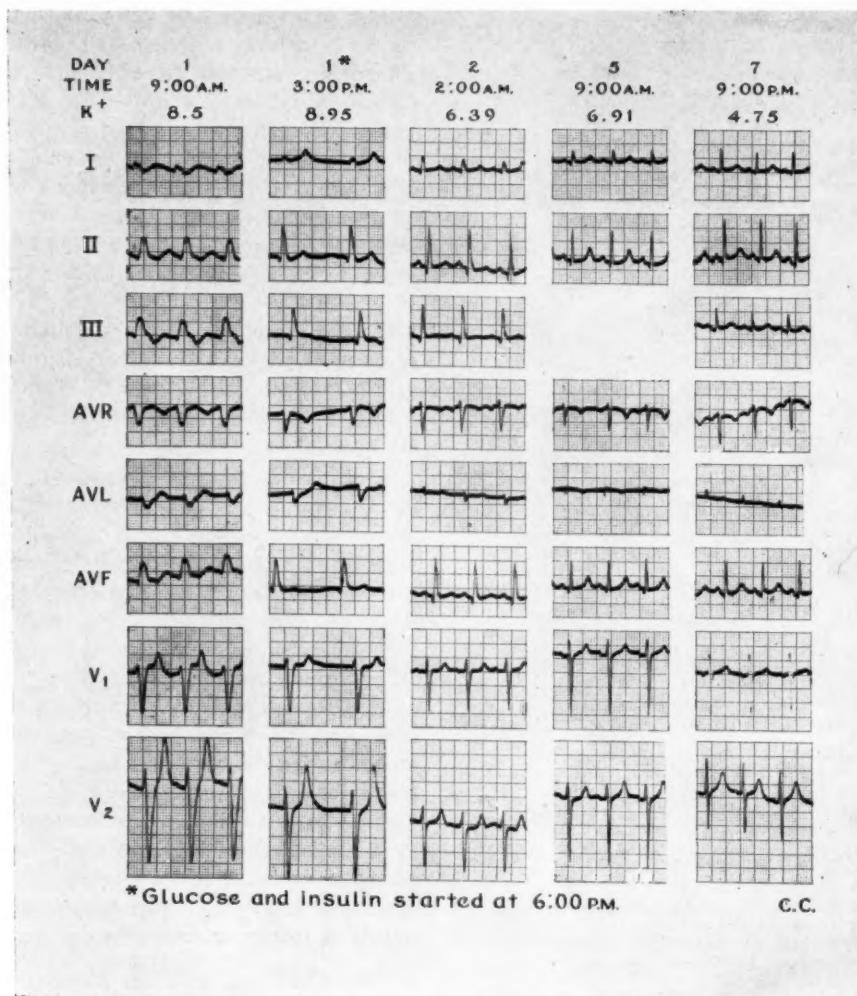


Fig. 1: This series of tracings records the progress of a patient who had anuria and hyperpotassemia. Note the wide QRS complexes in the first 2 tracings and the high and peaked T waves in the first 2 tracings in  $V_2$  especially. The K concentrations are recorded at the top. Note the progress of the electrocardiograms to normal as the serum potassium returned to normal.

significant clinical implications. The sum of sodium and potassium is 142-150 mEq/l. The last four items in the anion column are often not determined, are frequently as "R" and can be calculated by subtraction from the total cations. This process of calculating undetermined quantities by addition and subtraction is possible only when milliequivalents are used.

Chloride ( $Cl^-$ )	105 mEq/l	$= 608^*$ mg %
Bicarbonate ( $CO_3$ )	25 mEq/l	56 volumes %
Sum	130 mEq/l	?

One cannot add milligrams per cent and volumes per cent. There is no doubt that one can see that the figures are in the normal range with either

\*Reported as milligrams of NaCl per 100 cc.

## FLUID AND ELECTROLYTE BALANCE—FLINK AND ZIMMERMANN

method of notation and the sodium concentration cannot be far from normal under these circumstances. However, the following data derived from a case of metabolic alkalosis ac-

such quantitative information from the concentrations recorded in milligrams per cent and volumes per cent. Any number of such examples could be cited.

The bicarbonate and chloride concentrations cannot be used as a guide to the concentration of sodium in situations where either uremia or ketosis exists, for in ketosis there is an accumulation of organic acids which displace some of the bicarbonate so that if the sum of carbon dioxide and chloride concentrations were to be used as in the example above it would give an erroneously low estimate of cations. In uremia, retention of inorganic acid radicals ( $HPO_4^{2-}$  and  $SO_4^{2-}$ ) cause a similar displacement of  $CO_2$ . Uremia, incidentally, is one condition where expression of phosphorus concentration in terms of mEq/l is useful to indicate the significant contribution it makes to the anion column in this condition.

Most clinical laboratories can perform chloride and carbon dioxide determinations. Though the availability of sodium and potassium determinations is much more limited, the electrocardiogram furnishes a means of recognizing hyperpotassemia and hypopotassemia. Electrocardiographs are available in every hospital and are very valuable as guides to therapy with potassium and as a means of detecting both deficiencies and intoxication. Patterns of each extreme are distinctive as illustrated by Figures 1 and 2. The first of these shows the characteristic tracing in a patient with high potassium which is subsequently reduced by administration of glucose and insulin. The second gives the electrocardiographic features of potassium depletion. Figure 3 illustrates gradual transition toward normal.

### The Fluid Spaces: Their Boundaries and Constituents

The relative ease with which a sample can be obtained from the circulating blood inevitably results in the tendency of the clinician to describe abnormalities of fluid and electrolyte physiology in terms of the blood or plasma values with which they are associated. Although the value of such determination cannot be discounted, any rational consideration of the fundamentals of fluid and electrolyte physiology must take into account a consideration of all the major fluid spaces and the boundaries which separate them.

Conventionally, the fluid volume in which the

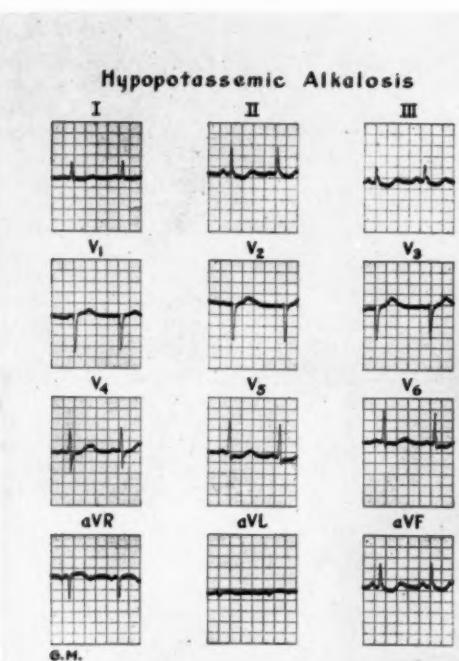


Fig. 2: This electrocardiogram records some of the abnormalities found in hypopotassemic states (not just hypopotassemic alkalosis). The QT interval is prolonged, the ST interval is depressed and the T wave is inverted diphasic in leads 2 and 3, there is often a prominent "U" wave (after the T wave) in  $V_2$  especially. Various degrees of heart block may also occur. The most significant findings are the prolonged QT and ST segment depression. (The apparent prolongation of the QT interval is actually due to blending of "U" wave with the "T" wave.)

centuates the difficulties involved with the older units.

(2)			
Chloride (Cl)	90 mEq/l	= 522 mg %	
Bicarbonate ( $CO_2$ )	40 mEq/l	= 89 volumes %	
Sum	130 mEq/l		?

In this example of some of the chemical findings in alkalosis it can be seen quite readily that the sum of major anions is normal and this gives the additional information that the major cation concentration (sodium) must also be approximately normal. There is no way of deducing any

soluble constituents of the body are distributed is divided into the intracellular fluid and the extracellular fluid, the latter being in turn composed of the blood plasma and interstitial fluid. The

siderably lower, probably in the neighborhood of 61 per cent for men and 52 per cent for women<sup>5</sup>. The difference is the result of the somewhat larger proportion of fat in the latter.

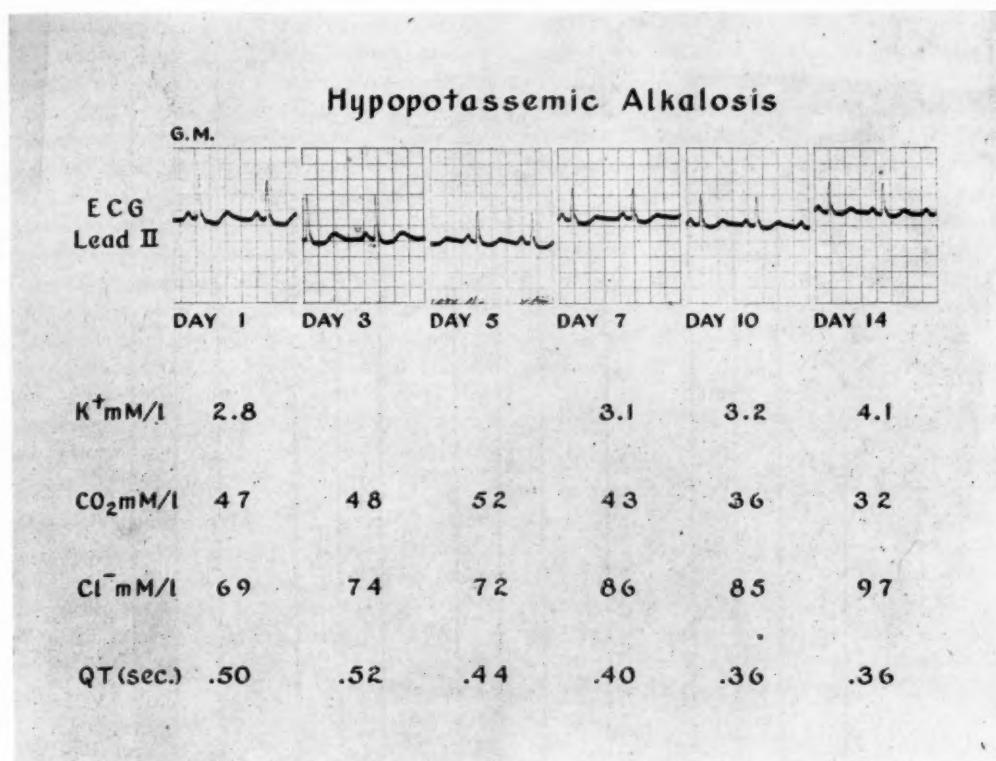


Fig. 3: A series of chemical determinations on serum and lead II of the electrocardiogram on the corresponding day are recorded. Note the gradual transition toward normal of the chemical findings and a return to normal of the electrocardiogram.

extracellular volume is usually given as 20 per cent of the body weight although this value varies quite widely depending on the methods of measurement which are used. The thiocyanate method gives a somewhat larger figure (23 per cent), whereas more recent methods such as inulin and thiosulfate which are believed to determine the extracellular space with greater accuracy give values of 17 per cent to 18 per cent. The intracellular fluid has been considered to comprise about 50 per cent of the body weight, so that the total body water for the adult human amounts to approximately 70 per cent of body weight. Here again more recent methods such as the use of heavy water for the direct measurement of total body water suggest that this value should be con-

The remarkable differences in the ionic composition of the two major fluid compartments are shown in Figure 4 which is reproduced from Gamble's Lane lecture.<sup>6</sup>

The blood plasma and interstitial fluid are essentially the same in composition except for the difference in concentration of protein which is much higher in the plasma. The composition of the cell fluid, on the other hand, is radically different from that of the extracellular fluid. The most striking difference is that sodium is the major extracellular cation and potassium occupies this position inside the cell. Although it was previously believed that sodium did not enter the cell, it has been definitely shown that small amounts of sodium, such as are represented on

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the diagram, are actually present. Chloride is a major extracellular anion and phosphate the predominant intracellular one. The question of whether there is ever any significant amount of

past, it was simply assumed that the cell membrane was impermeable to sodium ions. The application of tracer techniques, however, has shown that this is in no way the case, for the cell mem-

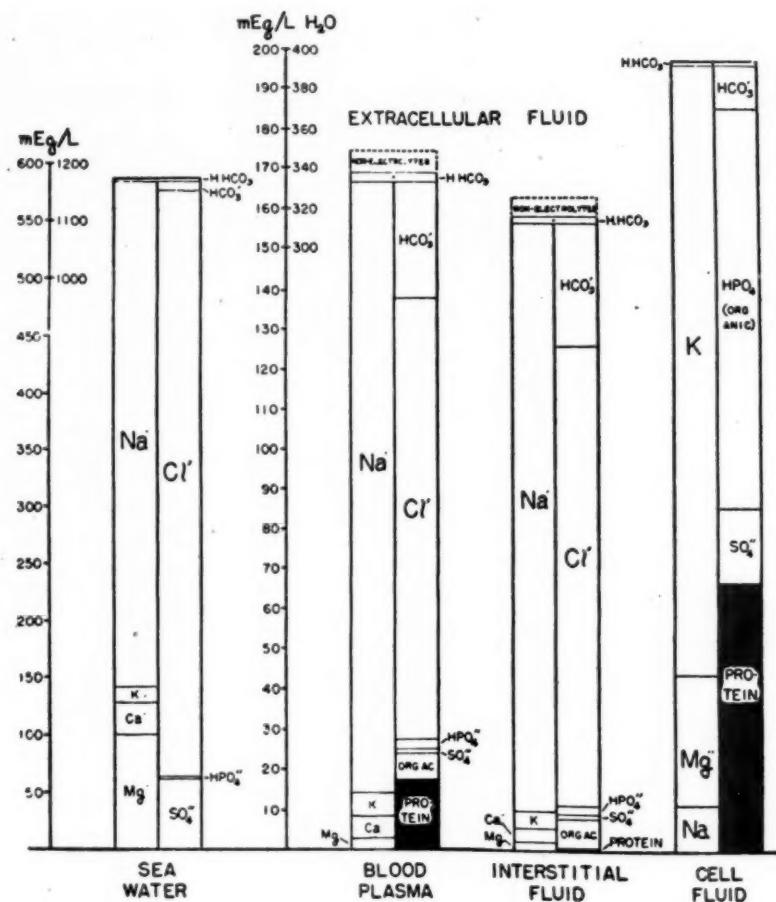


Fig. 4: Concentration of major constituents in blood plasma, interstitial fluid, intracellular fluid and sea water. Gamble, J. L., Lane Medical Lectures: Companionship of water and electrolytes in the organization of body fluids. Reproduced by consent of the author and the Stanford University Press.

chloride inside the cell under either normal or abnormal circumstances remains to be settled. Most calculations relating to the distribution of electrolytes in the body even under circumstances of disease are based on the assumption of the exclusively extracellular position of chloride. The mechanism by which this inequality of distribution of sodium and potassium is maintained represents a problem as yet largely unsolved, but one of intense interest to those concerned with the basic properties of living membranes. In the

brane is apparently freely permeable to sodium ion and the phenomenon cannot, therefore, be explained on the basis of membrane permeability alone. The fact is, that active processes within the cell are constantly working to extrude sodium and thereby maintain the extreme gradient across the cell membrane which normally exists. This process requires the expenditure of energy which is produced by cellular metabolism and, although numerous theories for the mechanism by which energy is utilized to maintain this gradient have

been proposed, the question is still an obscure one. Likewise the nature of the high intracellular potassium concentration with respect to the level in the extracellular fluid remains to be elucidated. The maintenance of these two extreme gradients across the cell membrane is surely one of the most fundamental processes of life and is as important to the normal function of living cells as the assimilation of oxygen and the transport of carbon dioxide. As will be discussed in the succeeding sections, recent studies of electrolyte changes during illness have shown that the great alterations from a normal intracellular-extracellular gradient of sodium and potassium can occur, the characteristic response, in most instances, being one of loss of potassium from the cell with entrance of sodium from the extracellular fluid to replace it. Thus, as might be anticipated, the characteristic of "sick cells" is the loss of ability to expend energy in the maintenance of these unequal concentrations and the production of an intracellular ionic pattern more closely resembling that of the medium by which the cells are surrounded.

The first column in Figure 4, which describes the composition of sea water, gives a clue to the background of the astounding relationship which exists between chemical components of the cell and those of the fluid which bathe it. It will be observed that the concentrations of extracellular fluid and sea water are remarkably similar except for few significant differences, most important of these being that the overall concentrations of salt is over three times as high in the sea as in mammalian extracellular fluid. The interpretation of this is that the internal environment of land creatures today is that which existed in the sea at the time when the prototypes of these animals emerged from the ocean millions of years ago. The progenitors of the vertebrates acquired a closed circulation and thereby segregated themselves from their oceanic environment in the early Cambrian era when the sea was much more dilute than it is now. Though the total salinity of the sea has greatly increased, the relationship of concentrations of the ions to each other has remained the same. The outstanding exception to this is the case of magnesium whose concentration has mounted much more rapidly. This principle was demonstrated by Macallum whose extensive studies of the extracellular fluid in many species established the relationship between ionic concentrations in the organisms as they exist today

and the calculated concentrations in sea water at the time their original prototypes acquired a closed circulation.<sup>1,8</sup> The principle is of more than amusing historical interest, for the characteristic of the ocean with its vast volume and complete immutability except for the changes wrought by millions of years is one of extraordinary constancy of both composition and physical qualities. Consequently, the basic requirement for cellular life which began in the sea is one of a constant fluid environment. This necessity for constancy is summarized in Claude Bernard's famous dictum which stated that constancy of the internal environment is the necessary condition for independent life.<sup>2</sup> The physiologic and pathologic principles with which these papers are to be concerned all revolve around the efforts of the body to maintain these conditions.

### The Regulation of Water and Fluid Spaces

Although the cell in a rigid sense is permeable to sodium ion, the fact that sodium is predominantly maintained in an extracellular position endows it with osmotic properties identical with those of a substance to which the membrane is actually impermeable. Thus sodium, being the major extracellular component, governs the major osmotic force which stabilizes the distribution of water between the cells and the extracellular compartments. This fact was first stated by Darrow and Yannet, who, in 1935, postulated that the volume of the cell was not sensitive to the overall extracellular volume but only to the total osmolarity (and therefore the concentration of sodium) in the extracellular fluid.<sup>3</sup> An increase in sodium concentration results in the movement of water from the cell and a consequent shrinking of cells until the osmolar concentrations of the two media are again in equilibrium. Conversely, a loss of sodium ions from the extracellular fluid results in an inward motion of water until a similar equilibrium is attained. Furthermore, addition of water with dilution of electrolytes has the same effect as removal of salt. The phenomenon is illustrated in Figure 5 by a diagrammatic representation of the changes in volume consequent to adding or subtracting 500 milliosmos of sodium chloride from the extracellular fluid compartment. As will be seen, these shifts of water may be the basis for clinical aberrations of the severest nature.

**The Regulation of Salt Balance**

In view of the fundamental relationship between extracellular sodium and intracellular volume it is important to consider the factors

along with much less and herein lies one of the most important homeostatic mechanisms of the kidney. Diets such as are given in the treatment of cardiac disease which contain as little as 200 mg

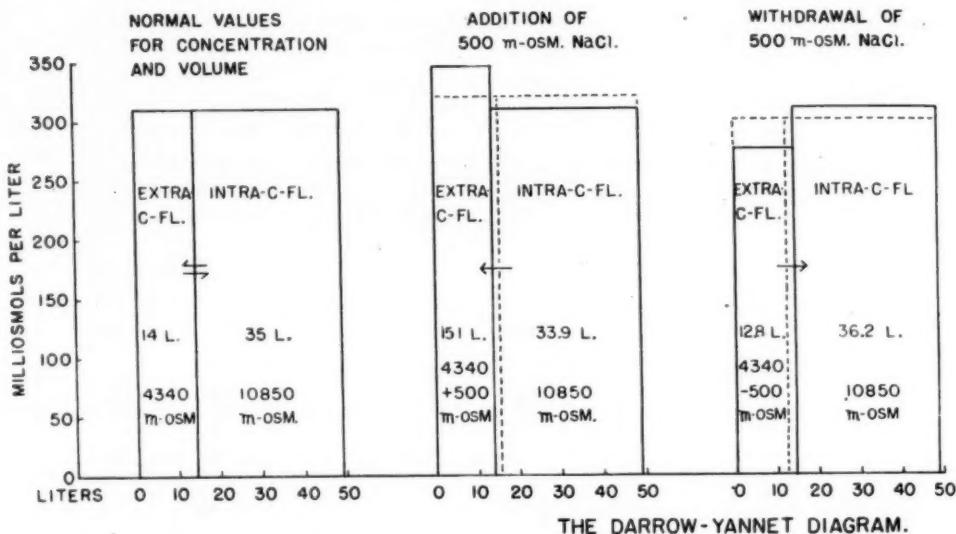


Fig. 5: The Darrow-Yannet diagram illustrating the effects on intracellular volume of adding or removing sodium from the extracellular fluid compartment. Reproduced from Gamble, J. L., Extracellular fluid, with kind permission of the author and the Harvard University Press.

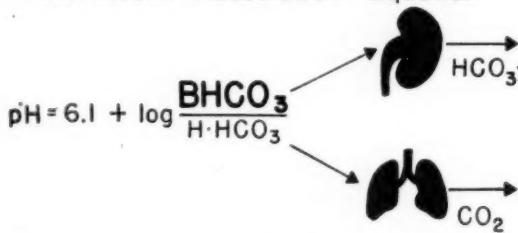
**Henderson-Hasselbach Equation**

Fig. 6: The Henderson-Hasselbach equation for the relationship between pH and the concentrations of carbonic acid and bicarbonate. This emphasizes that the normal concentration of bicarbonate is much greater than that of carbonic acid (ratio 20:1) and that the former is controlled mainly by the kidney, the latter being under control of the lungs.

which maintain the concentration of this ion in the extracellular fluid. Most human beings ingest considerable excesses of salt in the course of a day, intakes of three to six grams being common. For some reason our taste leads us to take far larger quantities of sodium chloride than are actually required. One can, on the other hand, get

of sodium may be tolerated for long periods of time. This results from the ability of the kidney to reabsorb nearly all of this ion from the glomerular filtrate and replace it in the blood stream for the maintenance of the proper extracellular concentration. This power for conservation of sodium does not obtain with respect to potassium which is put out in the urine in considerable amounts even when eliminated from the diet or when extracellular levels become seriously depressed. Though this difference of economy between sodium and potassium ions seems superficially unsound, we are again reminded of the circumstance that we are basically marine organisms highly adapted to the function of carrying our sea water environment around with us. The vertebrate land animal is endowed with the ability to maintain his sodium-salt environment in a world where potassium is abundant and sodium is precious and the herbivorous animal in particular can ingest sodium-salt only by actual visits to his watery ancestral home or by seeking the dried up remnants of the ocean which exist in the form of salt deposits.

### The Regulation of Acid-Base Balance—Acidosis and Alkalosis

Most critical of conditions for which constancy must be maintained in a tolerable environment for

bicarbonate is simply derived from the mass action law which describes the dissociation of an acid into its component ions. This formula which is known as the Henderson-Hasselbalch equation

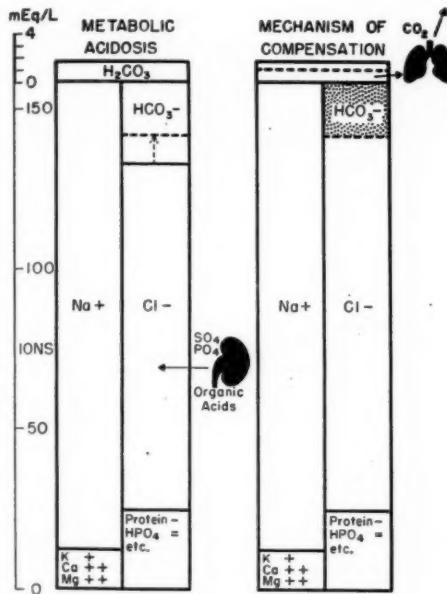


Fig. 7: Metabolic acidosis. Left: Primary disturbance caused by retention of acids by the kidney. Right: Compensation is achieved by hyperventilation and consequent decrease in carbonic acid.

living cells is that of the concentration of hydrogen ions. The pH is maintained within narrow limits in the normal plasma of from 7.35 to 7.42. The first line of defense in this regulation is the buffering power of the weak acid carbonic which exists in equilibrium with bicarbonate ions as shown below.



The combination is a buffer because when more hydrogen ions are added to the system, the equilibrium is shifted to the left, more  $\text{H}_2\text{CO}_3$  is formed and hydrogen ions thereby "absorbed." The relative amounts of carbonic acid and bicarbonate determine the pH and the situation is further stabilized since the concentrations of these two substances are controlled respectively by the lungs and the kidneys. The formula which relates the pH to the dissociation constant of carbonic acid and the existing ratio of carbonic acid to

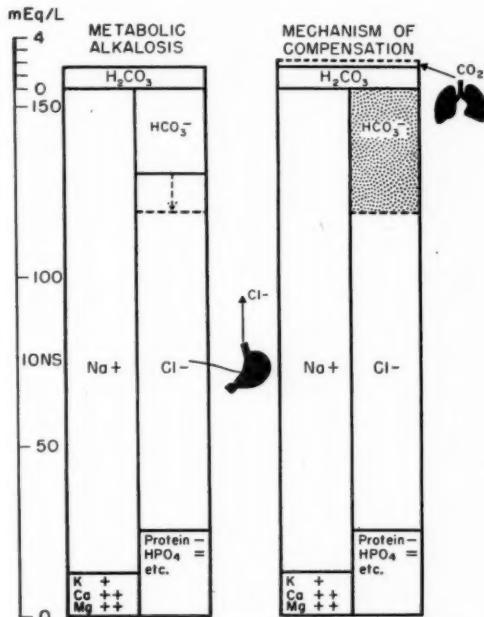


Fig. 8: Metabolic alkalosis. Left: Primary defect caused by loss of chloride through vomiting and consequent increase in bicarbonate. Right: Compensation is achieved by retention of carbon dioxide by the lungs and consequent increase in carbonic acid of the plasma.

is shown in Figure 6 in such a way as to demonstrate that the bicarbonate is present in much greater quantities than carbonic acid (the normal ratio is 20 to 1). It indicates, furthermore, that excesses of bicarbonate are handled by excretion through the kidney and carbonic acid is removed from the body by conversion to carbon dioxide and excretion through the lung.

Disturbances of acid-base balance are of two types: *Respiratory disturbances* in which the primary effect is on the carbonic acid or dissolved carbon dioxide of the blood with secondary or compensatory changes occurring in the bicarbonate ions, and *metabolic disturbances* in which the primary effect is on the bicarbonate ions with compensatory adjustments occurring in the carbonic acid. Since the regulation of carbonic acid is managed entirely by the lung it is apparent why respiratory disturbances should be manifested in

## FLUID AND ELECTROLYTE BALANCE—FLINK AND ZIMMERMANN

its concentration. Bicarbonate, on the other hand, is altered by metabolic disturbances because it is labile and its concentration is completely limited by the concentration cations which have not already been covered by other anions. The move-

characteristic breathing of acidosis results. Conversely, when the bicarbonate is increased through the mechanism of chloride loss, a decreased depth and rate of respiration must take place in order that an accumulation of carbonic acid can balance the accumulation of bicarbonate. Since the final value of the bicarbonate is the value which is actually measured clinically, this value is shown as a stippled area in each of the diagrams.

The majority of disturbances of acid-base equilibrium which are clinically seen are of the metabolic type. Nevertheless, respiratory disturbances are not uncommon and are receiving increasing interest, for example, in connection with thoracic surgery, and inhalation anesthesia. Figure 9 illustrates the situation in disturbances of primary respiratory origin. A decreased ventilation results in accumulation of carbonic acid and the result is respiratory acidosis.

In response to this situation the kidney stops excreting bicarbonate and along with this, in order that the sodium concentration may be maintained, begins to excrete excessive amounts of chloride. The situation is therefore partially compensated by altering the numerator of the fraction in the same direction that the denominator has been changed. The result is a high bicarbonate. The point is that in the compensated situation the bicarbonate is high in both metabolic alkalosis and respiratory acidosis. A measurement of the bicarbonate alone, therefore, or of the carbon dioxide combining power which is usually done in hospitals as a measurement of the bicarbonate, will not distinguish between these two conditions and in order to make this distinction one must have an actual measurement of the pH or at least must have clearcut clinical information as to whether the patient is suffering primarily from a metabolic or a respiratory derangement. Fortunately, the latter information is usually available and it is only in the unusual situation that the physician does not know on clinical grounds which type of disorder is present. Consider then the situation when through nervousness or other mechanisms the patient begins to hyperventilate (Figure 10).

Carbon dioxide is removed and the carbonic acid drops to a low value. Respiratory alkalosis results and the compensation consists in the excretion of large amounts of bicarbonate by the kidneys with a corresponding retention of chloride. Here again a measurement of the bicar-

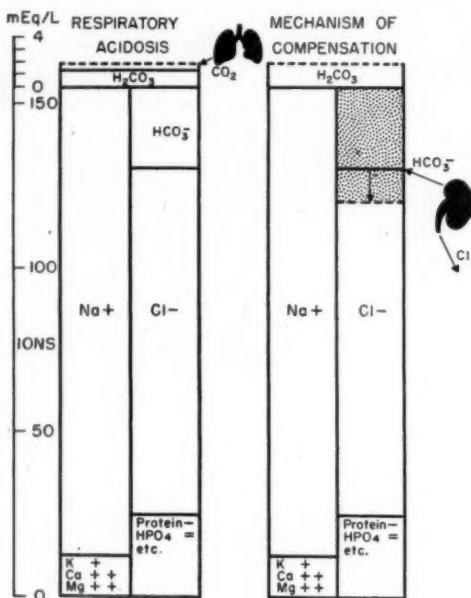


Fig. 9: Respiratory acidosis. Left: Primary defect caused by retention of carbon dioxide due to respiratory impairment. Right: Compensation is achieved by retention of bicarbonate and excretion of chloride by the kidney.

ment of bicarbonate in response to changes in other anions is therefore illustrated in Figure 7 in which the acidosis resulting from failure of excretion of anions in uremia (sulfate, phosphate, and acids) results in a decrease in bicarbonate concentration.

Figure 8 shows the converse situation: an alkalosis is produced by a loss of chlorides through vomiting and is reflected in an increase in bicarbonate concentration.

Consider now the respiratory compensation to these two situations. The effort of the body is, insofar as possible, to return to the normal 20 to 1 fraction of bicarbonate to carbonic acid. If, therefore, bicarbonate decreases as in the situation described for metabolic acidosis, carbonic acid must be decreased as well and this is accomplished by increasing ventilation in order to allow an escape of carbon dioxide by decreasing the concentration of this gas in the alveolae. The

bonate or the  $\text{CO}_2$  combining power is not a basis for distinction between the depressed values which are characteristic of both respiratory alkalosis and metabolic acidosis. Fortunately again, in most clinical situations the necessary facts are known. Occasionally, however, a determination of pH must be done.

Whereas, the buffering capacity of the blood is responsible for the fine adjustment of the hydrogen ion concentration, the main work of relieving the body of great excesses of acid or alkali is achieved by the kidney. The most continual problem is the removal from the body of large amounts of acid which are discharged from the cells as a result of the oxidation processes of metabolism. The removal of acid is made possible by the fact that urine can be produced at a pH far lower than can be tolerated in the blood. The excretion of such an acid with the conservation of base (cations) is made possible by two mechanisms:

1. Whereas, phosphate ion exists in the blood ordinarily in the form of its dibasic ion and covers two cationic equivalents, it is excreted by the kidney in the monobasic form with corresponding conservation of positively-charged ions.

2. The kidney produces ammonium ions ( $\text{NH}_4^+$ ) for excretion with acid radicals with resultant conservation of important cations such as sodium. As will be seen later the acidosis which results from renal damage involves both the failure to excrete acid radicals and a breakdown in the mechanism for conserving sodium.

### The Regulatory Effect of Hormones

Increasing attention in recent years has been directed towards the regulatory effect exerted by hormones on the balance of salt and water. This is a most important subject about which a great deal remains to be learned. Hormones are never entirely responsible for any single physiological phenomenon. All available evidence appears to indicate that in every vital process, which endocrine substances influence, the basic enzymatic pattern exists in the cells themselves, the hormones only acting as catalysts whose function is to regulate the rate of the reactions concerned. This concept does not contradict the obvious fact that such regulation is frequently necessary to

life. An example of this is the re-absorption of sodium by the renal tubules which is not far from being completely absent following adrenalectomy but is vastly intensified in the presence of these glands.

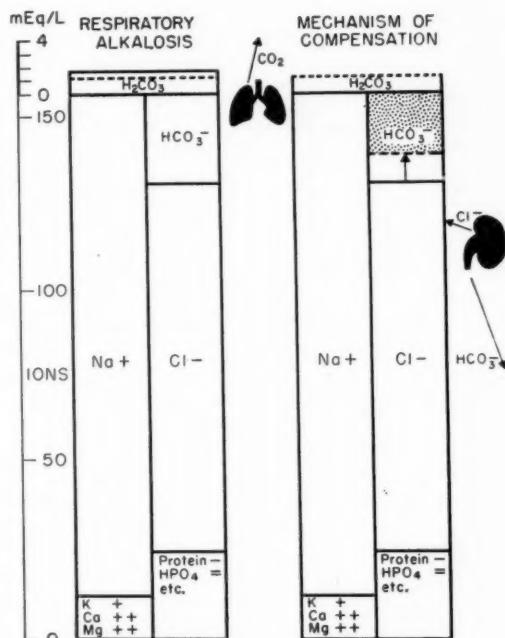
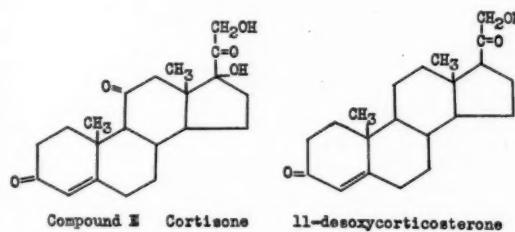


Fig. 10: Respiratory alkalosis. Left: Primary defect resulting from increased ventilation and loss of carbon dioxide resulting in decreased carbonic acid. Right: Compensation is achieved by excretion of bicarbonate and retention of chloride by the kidney.

**The adrenal cortex:** The adrenals produce a variety of hormones of which two groups, the glucocorticoids and the mineralocorticoids are illustrated below by their prototypes, cortisone and 11-desoxycorticosterone.



These two substances are chosen as models because they are familiar compounds the pharmacologic actions of which are well known and not

## FLUID AND ELECTROLYTE BALANCE—FLINK AND ZIMMERMANN

because they are produced in the greatest amounts by the adrenal gland. As a matter of fact, desoxycorticosterone has been obtained in only very minute quantities from adrenals and this precise compound by itself may have little or no significance normally as an adrenal hormone. In general, the first group of substances are identified mainly with a metabolism of protein and carbohydrate, the second group being concerned with the handling of electrolytes. Nevertheless, the distinctness of these actions is by no means complete, and there is a good deal of overlap of functions. The typical effect, for example, of the adrenal hormones on sodium and potassium metabolism is to cause retention of sodium ion and increase excretion of potassium. This general phenomenon varies very widely between the substances and is much more pronounced in relationship to compounds like desoxycorticosterone. Nevertheless, the pronounced tendency toward sodium retention and potassium loss is also a familiar clinical phenomenon during treatment with cortisone and the frequent necessity for employing a low sodium diet with addition of excess of potassium during such treatment is now well recognized. The effects of these substances on the metabolism of water is complex. The accumulation of edema fluid during chronic administration of adrenal materials is significant and is frequently demonstrable clinically. Nevertheless, if one considers the effect of these hormones on the balance of water alone it is primarily one of diuresis.<sup>7</sup> Thus, the Robinson-Power-Kepler water test is used to diagnose adrenal insufficiency by demonstrating the inability of the individual to respond to a load of water.<sup>11</sup> These effects on both electrolyte metabolism and water balance are important not only because of the frequent use of these substances in present-day therapy but also because of the increase in adrenal activity which is known to accompany injury and disease. These specific problems with which they are believed to be associated will be discussed later particularly in connection with electrolyte problems of surgery. It is important to recognize also that the effects of adrenal hormones on salt and water are not exclusively related to the activity of the kidneys. Extrarenal influences on the distribution of sodium and potassium across cell membranes have been demonstrated in nephrectomized animals and are surely of importance in the shifts of electrolytes known to occur

in disease. Thus, the effect of either adrenal treatment or adrenal stimulation is to cause a loss of potassium from the cell with a concomitant gain in intracellular sodium. The overall effect of this, which is to produce a metabolic alkalosis, will be discussed more fully in the sections dealing with potassium deficiencies.

What mobilizes these materials from the intact adrenal in the physiological adjustment of the healthy individual? The glucocorticoids are released from the adrenal in response to the pituitary corticotrophic hormone (ACTH). The pituitary, in turn, is stimulated by the hypothalamus and there is some evidence that the pituitary is also sensitive to the circulating levels of adrenal steroids and can respond by secreting more ACTH when there is a drop in plasma-steroid concentrations. Almost nothing is known, however, as to the mechanisms which control the production and release of substances specifically concerned with salt retention. The pituitary corticotrophic mechanism is apparently not involved in this as shown by the fact that ingestion of a diet designed to call forth the production of "salt-retaining adrenal hormones" does not result in evidence of increased corticotrophic production.<sup>12</sup> Many investigators feel that the adrenal in this respect is directly sensitive to the sodium-potassium ratio of the blood. It must be appreciated, furthermore, that we really do not know the chemical nature of the most important salt-retaining adrenal hormones. It was mentioned above that desoxycorticosterone was probably not a significant naturally occurring substance. Recent chemical extraction of adrenal glands by Reichstein in Switzerland and Mason in this country have resulted in the discovery of substances as yet chemically unidentified which are far more active than desoxycorticosterone on sodium retention in the rat.<sup>9,10</sup> The occurrence of such substances in human subjects are currently being investigated, and it would appear, therefore, that within a few years we should know much more about the true nature of the endocrine regulation of sodium and potassium metabolism.

*Posterior pituitary:* Finally, in this connection, consideration should be given to the posterior pituitary, a special adaptation in the vertebrate which, through control over the absorption of water in the distal tubule, is able to cause the ex-

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cretion of the urine which is hypertonic with respect to the blood. The regulation of the secretion of this hormone is of particular interest since, as has been shown by Verney, there are in the ramifications of the circulation to the brain, receptors which are sensitive to tonicity of the blood.<sup>12</sup> The stimulation of these by hypertonic concentrations apparently stimulates the release of antidiuretic hormone which in turn affects retention of water by the kidneys. Except in the case of diabetes insipidus wherein the effect of the posterior pituitary is completely removed the significance of this gland in disease remains largely to be explored. Part of the difficulty lies in the fact that only biological methods of assay are available for this substance and there would be no question that the development of chemical methods of analysis would be a great stimulus to the study of this field. Nevertheless, with present methods it would appear that in certain diseases such as cirrhosis, excessive amounts of antidiuretic hormone are circulating. Similar observations have been made regarding postoperative surgical patients.

### References

1. Baldwin, E.: Introduction to Comparative Biochemistry. University Press. Cambridge, 1940.
2. Bernard, C.: *Leçons sur les phénomènes de la vie communs aux animaux et aux végétaux*. Paris: J. B. Ballière et fils, 1878.
3. Darrow, D. C., and Yannet, H.: The changes in the distribution of body water accompanying increase and decrease in extracellular electrolyte. *J. Clin. Investigation*, 14:226, 1935.
4. Davenport, H. W.: The ABC of Acid-Base Chemistry. 3rd Edition. University of Chicago Press, 1953.
5. Edelman, I. S., Holly, H. B., Schloerb, M. D., Sheldon, D. B., Friis-Hansen, B. J., Stole, B., and Moore, F. D.: Further observations on total body water. I. Normal values throughout the life span. *Surg., Gynec. & Obst.*, 95:1, 1952.
6. Gamble, J. L.: Companionship of water and electrolytes in the organization of body fluids. *Lane Medical Lectures*, Stanford University Press, 5:1, 1951.
7. Gaunt, R., and Birnie, J. H.: Hormones and Body Water. Springfield, Illinois: Charles C Thomas, 1951.
8. Macallum, A. B.: The paleochemistry of the body fluids and tissues. *Physiol. Rev.*, 6:316, 1926.
9. Mattox, V. R., Mason, H. L., and Albert, A.: Isolation of a sodium-retaining substance from beef adrenal extract. *Proc. Staff Meet. Mayo Clin.*, 28: 569, 1953.
10. Reichstein, T.: Data presented at International Congress of Rheumatic Diseases, Geneva, August, 1953.
11. Robinson, F. J., Power, M. H., and Kepler, E. J.: Two procedures to assist in the recognition and exclusion of Addison's disease. *Proc. Staff Meet. Mayo Clin.*, 16:577, 1941.
12. Verney, E. C.: Absorption and excretion of water. The antidiuretic hormone. *Lancet*, 2:739, 1946.
13. Zimmermann, B., and Schoenbauer, M. M.: Studies on the Control of Salt-Regulating Adrenal Hormones. *Surgical Forum*. Philadelphia: W. B. Saunders Company, 1952.

### EARLY TREATMENT INCREASES SURVIVAL CHANCES IN HODGKIN'S DISEASE

The importance of early diagnosis and treatment is clearly brought out by research figures based on irradiation therapy of 208 patients with Hodgkin's disease, according to Dr. Charles M. Nice, a radiologist, and K. Wilhelm Stenstrom, Ph.D., a radiation physicist, in a paper published in the May, 1954 issue of *Radiology*.

Their conclusions stem from research done at the University of Minnesota Medical School, department of radiology.

A series of 208 patients with proved Hodgkin's disease showed a five-year overall survival rate of 25 per cent. For 167 patients followed ten years or longer, the ten-year overall survival rate is 11 per cent.

"Clinical staging," the authors report, "is the most accurate aid in prognosis and is necessary in comparing series from various medical centers."

Their research conclusions were based on the clinical classification into three stages devised by M. V. Peters.

For twenty patients in Stage I, the five-year survival rate is 85 per cent; for thirteen of these, followed ten

years or longer, the ten-year survival rate is 77 per cent. In Stage II, there is 90 per cent survival for twenty patients followed five years and a 35 per cent survival rate for seventeen patients followed ten years.

"Thus, the difference between Stages I and II is shown in the ten-year period," the authors write.

In the much larger group comprising Stage III, representing those patients with disseminated disease, the five-year and ten-year survival rates are 10 and 3 per cent respectively.

General conclusions advanced, based on the research:

- (1) In Stage I, the treatment of choice is either intensive irradiation or, possibly, surgical excision followed immediately by intensive irradiation.
  - (2) In Stage II, intensive irradiation is the treatment of choice.
  - (3) In Stage III, palliative irradiation to reduce tumor masses or relieve symptoms is indicated.
- "It is in the latter group that the nitrogen mustards and triethylene melamine may serve as useful adjuncts," the authors conclude.

## FLUID AND ELECTROLYTE BALANCE

### II. Parenteral Fluid Therapy in Infants and Children

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IN THE preceding paper of this symposium, Flink and Zimmermann<sup>9</sup> discussed in some detail the fundamentals upon which a rational program of fluid and electrolyte therapy must be based. They have outlined and defined the terminology, physiology, and primary disturbances of body water and electrolytes. These basic considerations warrant careful study by the physician who intends to make use of the advances in therapy resulting from recent studies in this field.

The treatment of any patient who is in need of parenteral fluid therapy requires an understanding of the way a particular disease affects fluid balance and electrolyte composition. In addition, the treatment of infants and children necessitates a knowledge of the different requirements for water and electrolytes that result from differences in size, metabolic rate, and kidney function.

It is not possible to translate therapy as used in the adult directly to the child. Because of differences in size, the quantity of fluid that is correct for an adult is obviously too much for a small child; however, because the higher metabolic rate produces a relatively greater water requirement in the child, a quantity of fluid and electrolytes calculated from adult values, using body weight as a guide, will often be inadequate for the child. Therefore, correct therapy must consider not only the size, but also the relatively higher requirements of the infant or child in need of such therapy.

The quantity of fluid required may be calculated on the basis of weight if a different value in milliliters per kilogram or milliliters per pound of body weight is used for various age groups. A simpler method is to use the surface area of the body as a guide (i.e. cc/m<sup>2</sup>), since surface area is closely correlated with metabolism and renal function. In this way requirements can be calculated without reference to size or age—the small child having the same requirement in milliliters per square meter of surface area as

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the adult. Customarily the surface area of the body is calculated by the use of the formula  $M^2 = \sqrt{(W)^2} \times 0.10$ , in which  $M^2$  = square meters surface area,  $(W)^2$  = the square of the value of the weight in kilograms. However, for simplicity the values for surface area, weight and twenty-four-hour fluid requirement may be obtained by use of the convenient graph in Figure 1.

Water comprises a greater proportion of the total body weight in the infancy period than at any other time. In the infant, approximately 75 per cent of the total body weight is water;<sup>12</sup> this percentage decreases to the adult value of 60 to 65 per cent at about two years of age. The extra water of the infant is located in the interstitial compartment (Fig. 2). The large interstitial compartment functions as a buffer, to prevent the relatively large intake and excretion of water from producing drastic changes in plasma volume. Although this large volume would seem to protect the infant against plasma volume depletion, it is more than offset by the higher rate of water loss, and so offers very little protection.

The necessity for increased fluid intake and excretion renders the infant, who is deprived of water—or who loses water as a result of disease, much more liable to dehydration and circulatory collapse than the adult. Therefore, diseases leading to dehydration require more vigorous treatment in the young child than in the adult.

The rate of turnover of body water is relatively greater in the infant because the higher rate of metabolism demands a higher urine volume to excrete the metabolic waste products, and because the relatively larger surface area produces greater losses of water from insensible perspiration and sweat. An understanding of the amount of water and electrolytes necessary to replace the normal losses will serve as a basis for understanding the amounts necessary to treat dehydrated patients.

The quantity of these normal losses is expressed in terms of surface area, so it can be applied to patients of any size.

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**Routes of Fluid Loss**

(a) *Loss as insensible perspiration*—via the skin and lungs: This loss is dependent upon temperature regulation and body surface area, not

without fever loses approximately  $600 \text{ cc/m}^2/24 \text{ hrs.}$ , as insensible perspiration.

(b) *Loss as sweat*: Sweat loss also depends largely upon temperature regulatory mechanisms

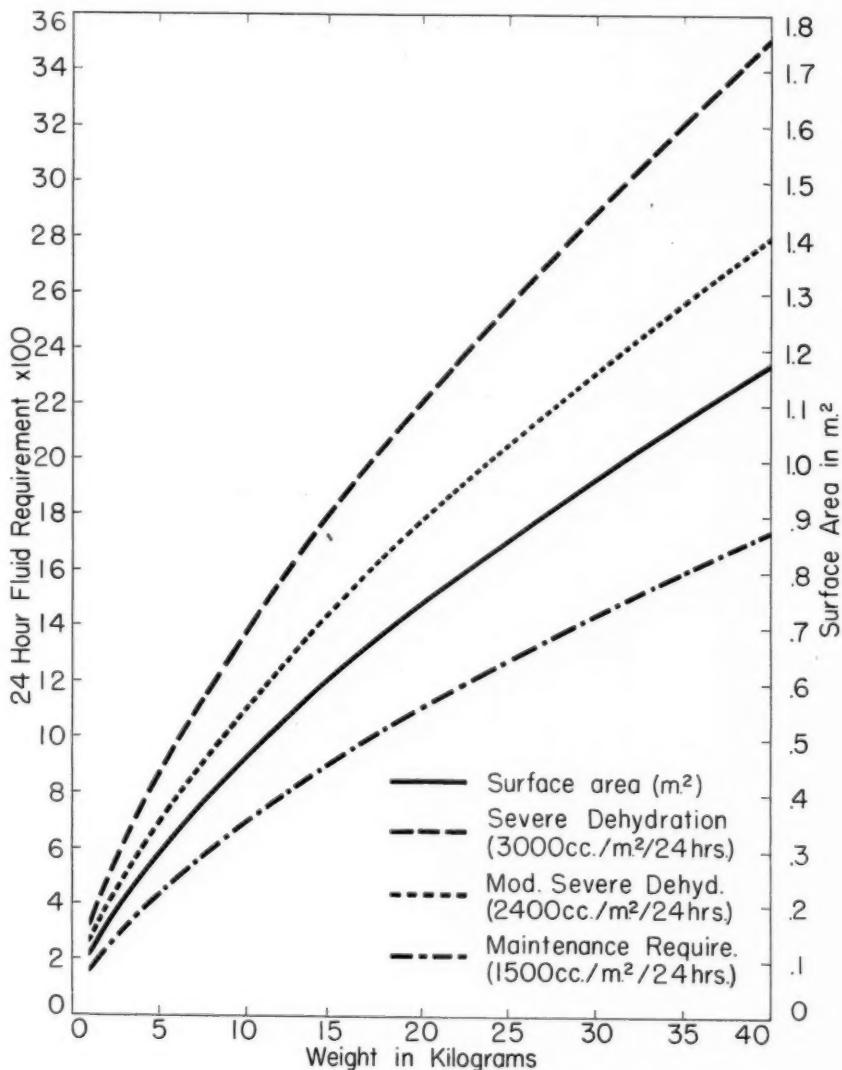


Fig. 1. Twenty-four-hour fluid requirements for three situations. The requirement in  $\text{cc}/24 \text{ hrs.}$  is found at the intersection of the patient's weight and the line appropriate for the patient's state of hydration.

on fluid balance. It is essentially continuous, and varies with the patient's temperature, and with environmental temperature and humidity. Under basal conditions, this loss approximates  $500 \text{ cc/m}^2/24 \text{ hrs.}$ <sup>14</sup> The average patient on bed rest

and environmental conditions. This loss varies from 0 to 3 Liters/ $\text{m}^2/24 \text{ hrs.}$ ,<sup>1</sup> depending upon environmental temperature and humidity.

(c) *Loss in stools*: Stool water normally averages 100 to 150  $\text{cc}/\text{m}^2/24 \text{ hrs.}$  In diarrheal

states the loss may be more than 1,000 cc/m<sup>2</sup>/24 hrs. In a patient not receiving oral fluids and without diarrhea the losses are usually minimal and can be ignored.

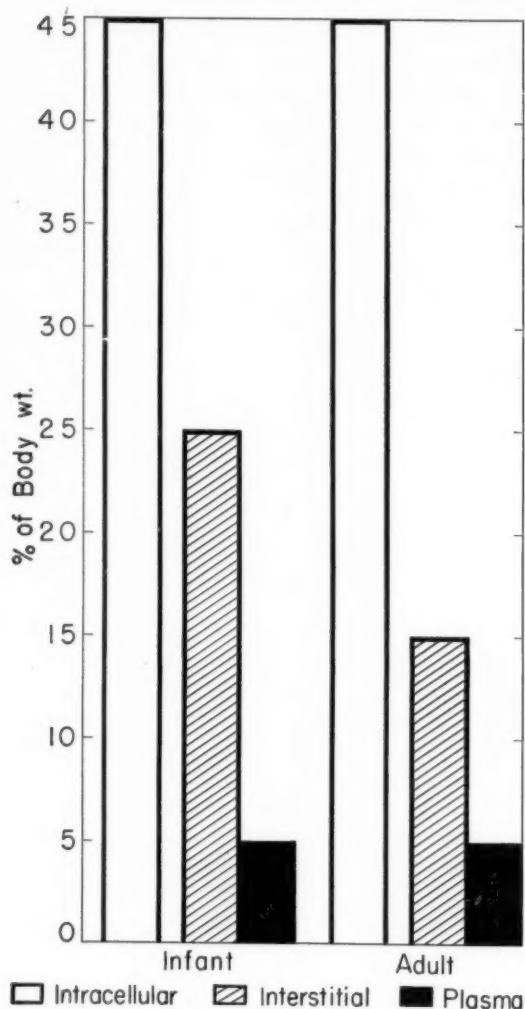


Fig. 2. Comparison of the volume of the fluid compartments in the infant and the adult, expressed as percentage of body weight.

(d) *Loss in urine:* The kidney is the most important regulator of water and electrolyte balance. The amount of urine excreted depends upon the concentrating ability of the kidney and the amount of solute requiring excretion. Minimum urine volume therefore occurs when concentration is maximal and solute load is minimal. In a healthy person, maximum concentration is approximately

1.4 m-osm/cc (Specific Gravity 1.030).<sup>11</sup> However, in a person under the stress of severe illness the maximum concentration may be only 0.4 m-osm/cc (Specific Gravity 1.012).<sup>4</sup>

The amount of solute that must be excreted depends upon the rate of catabolism of body tissues, especially protein, and the amount of exogenous solute furnished by the diet or parenteral fluids. The minimum solute excretion of 200 m-osm/m<sup>2</sup>/24 hrs. occurs when no food other than carbohydrate is given.

The least amount of glucose which will prevent ketosis and minimize protein breakdown is 75 gms/m<sup>2</sup>/24 hrs.<sup>5,10</sup> The maximum amount that can be given without causing glycosuria and adverse osmotic effects from hyperglycemia is approximately 300 gm./m<sup>2</sup>/24 hrs.<sup>2</sup> The minimum urine volume necessary to excrete 200 m-osm is 140 cc, if the patient can concentrate to a specific gravity of 1.040, and 500 cc if his concentrating ability is limited to a specific gravity of 1.012.

#### Sources of Water

In addition to the water administered, water is derived from catabolism of body tissue and from oxidation of food. When 5 per cent glucose is given as the only nutrient, in amounts of 75 to 300 gms./m<sup>2</sup>/24 hrs. the average amount of water derived from oxidation and catabolism will approximate 250cc/m<sup>2</sup>/24 hrs.<sup>5,10</sup>

*Maintenance Water Requirement.*—In a patient who is not dehydrated and who has no unusual losses, the minimum amount of water necessary to supply maintenance needs is equal to the water normally lost minus the water derived from oxidation and catabolism:

Insensible loss.....	600 cc/m <sup>2</sup> /24 hrs.
Stools .....	100-150
Urine .....	200-500
Minus the water of oxidation...	250
	750-1000 cc/m <sup>2</sup> /24 hrs.

Most patients who require parenteral fluids have fever and move about in bed, and are therefore not under basal conditions. In such cases the insensible water loss and sweat loss are increased. An approximation of the water requirement for maintenance in a sick person would be 1500 cc/m<sup>2</sup>/24 hrs.

### Limits of Electrolyte Tolerance

Parenteral fluid therapy with glucose solution only, is rarely indicated, since in almost any condition leading to a need for water, there exist electrolyte deficits also. Electrolyte deficits can be repaired more accurately if the physician understands the minimum electrolyte requirements and the maximum amounts that can be tolerated.

(a) *Sodium:* A healthy person is able to maintain sodium balance with as little as 10 meq./m<sup>2</sup>/24 hrs., and can tolerate loads to 700 meq./m<sup>2</sup>/24 hrs.<sup>15</sup> A person under the stress of acute illness tends to retain sodium, probably as a result of adrenocortical hormone action upon the kidney. Under such circumstances the maximum amount of sodium that can be tolerated may decrease to 250 meq./m<sup>2</sup>/24 hrs.

The amount of sodium that is to be given a patient should therefore fall within the limits of 10 to 250 meq./m<sup>2</sup>/24 hrs.<sup>16</sup> A reasonable amount for such purposes in the ill patient is from 50 to 150 meq./m<sup>2</sup>/24 hrs.

(b) *Potassium:* The limits of tolerance for potassium are from 10 meq./m<sup>2</sup>/24 hrs. to 250 meq./m<sup>2</sup>/24 hrs.<sup>8</sup> Since "stress" results in increased potassium excretion, as well as decreased sodium excretion, it is readily conceivable that an ill patient, given sodium but not potassium, may rapidly develop potassium depletion. If oliguria is present, however, the excretion of potassium is limited, and even small doses of potassium may produce a toxic concentration in the blood. It is absolutely necessary that the adequacy of circulation and urine formation be established before solutions containing potassium are added to a treatment regime.

(c) *Chloride:* The limits of chloride tolerance are not well defined. The amount of chloride needed will depend on the acid-base balance of the patient. Unless severe alkalosis is present, about two-thirds of the anion should be given as chloride; the rest as lactate.

(d) Other electrolytes such as phosphorus, calcium, and magnesium are usually disregarded in short term maintenance regimes unless there is evidence of specific deficits.

Only in recent years has the need for using potassium as a vital part of parenteral fluid therapy been recognized. Formerly, it was be-

lieved that only the extracellular electrolytes were affected, and that losses from the intracellular space involved only water. Darrow,<sup>7</sup> using balance studies in patients with diarrhea, found that potassium was lost as well as sodium and chloride. He demonstrated that the mortality could be decreased by furnishing potassium in the repair solution. The need for potassium has been demonstrated also by Butler,<sup>8</sup> in diabetic acidosis, by Lowe et al<sup>13</sup> in surgical patients, and by Danowski et al<sup>16</sup> in pyloric stenosis.

The depletion of cellular potassium in conditions causing either acidosis or alkalosis is apparently due both to increased urinary excretion of potassium, and to replacement of cellular potassium by sodium. The entrance of sodium into the cell and the loss of potassium seems to be the primary abnormality; the augmented urine potassium excretion reflects the increased potassium available because of its extracellular location.

In infantile diarrhea, for example, acidosis is not due primarily to the sodium lost from the body, since the chloride loss is equal to the sodium loss, but to the shift of a portion of extracellular sodium into the cell, in exchange for potassium. The potassium is excreted, and there remains an excess of extracellular chloride. If solutions containing sodium but not potassium are given, more potassium is forced out of the cell, and a severe or even fatal potassium deficiency may ensue. This explains why sodium lactate and sodium bicarbonate solutions will correct the low serum bicarbonate, but often actually make the patient worse. When potassium is supplied along with sodium, cellular potassium is repleted. The extracellular sodium is restored by the sodium given plus the sodium leaving the cell when potassium enters.

Most of the illnesses leading to dehydration cause a loss of fluid with an electrolyte concentration either isotonic or hypotonic as compared to plasma. At the same time, water is being lost by the insensible routes. Therefore, the usual type of dehydration encountered in practice will be hypertonic dehydration. Because of the hypertonicity of the extracellular space, water is shifted from the intracellular space, leading to intracellular as well as extracellular dehydration. The situation, when treatment is begun, is, therefore, hypertonic dehydration of both the intracellular and the extracellular spaces, lowered in-

intracellular potassium, and increased intracellular sodium. For this situation, a hypotonic solution containing both potassium and sodium is specific. The water given in excess of electrolytes restores hydration and corrects the hypertonicity, and the electrolytes furnish correct deficiencies in both the intracellular and extracellular compartments.

This type of solution is also well suited for furnishing the maintenance requirements of non-dehydrated patients who must receive parenteral fluids. The free water supplied will replace that lost by the insensible routes, and the electrolytes replace those lost in the urine and sweat.

Actually, even hypotonic dehydration, if not too marked, will respond very well to a hypotonic electrolyte solution. The normal kidney can form urine which is dilute enough to excrete much of the administered water with only a small portion of the administered electrolyte. The electrolyte depletion is repaired by selective retention by the kidneys.

### Approach to Fluid and Electrolyte Therapy

In treating patients with dehydration, the amount of fluid needed to restore normal hydration can be calculated by estimating the extent of the deficit that has occurred due to the illness and adding to this the maintenance requirement. If continued extra losses occur during treatment this amount is added to the total requirement.

Since it is very difficult to estimate with any degree of accuracy the amount of dehydration that exists in a given patient, and even more difficult to estimate the extent of electrolyte losses, advantage can be taken of the kidney's ability to retain needed water and electrolytes and excrete excesses. The patient is, therefore, supplied with water and electrolytes in excess of maintenance requirements in the form of hypotonic electrolyte solution. The correction then rests upon the wisdom of the kidney rather than upon the rough guess of the physician.

The amount of fluid needed in excess of the maintenance requirements will depend upon the extent of dehydration, whether mild, moderate, or severe. The type of fluid to be given will depend somewhat upon the specific disease state, but the vast majority of conditions can be satisfactorily treated with a hypotonic multiple electrolyte solution.

In a recent paper, Talbot et al<sup>16</sup> explained in detail the rationale for this treatment. The body

has limits within which it can handle administered fluid and electrolyte. If the amount of fluid and electrolyte given falls within these limits, and circulatory adequacy and renal function are established, the kidney will act to conserve what is needed and allow the remainder to be excreted. It is wise in practice to use amounts nearer the lower limits rather than the higher limits of tolerance, thereby decreasing the excretory burden upon the kidney.

The administration of the hypotonic solution at the rate of 2400 cc/m<sup>2</sup>/24 hrs., to a patient who is moderately dehydrated, will furnish enough water and electrolyte in excess of maintenance needs to correct a large portion of the deficit within the first twenty-four hours. A severely dehydrated patient may require 3000 cc/m<sup>2</sup>/24 hrs.

In the Department of Pediatrics of the University of Minnesota Hospitals, an intravenous fluid therapy program, based upon the rationales described above, has been satisfactorily used for the past seven years.

The electrolyte solutions used are:

#### 1. Initial Hydrating Solutions

(a)  $\frac{1}{3}$  isotonic saline,  $\frac{2}{3}$  5 per cent Dextrose in distilled water.\*

This solution is designed to furnish free water with electrolyte to restore hydration and urine output to a point where potassium-containing solutions can be safely used.

(b)  $\frac{1}{3}$  isotonic saline,  $\frac{2}{3}$  5 per cent Dextrose in distilled water, with 26 ml. Molar sodium lactate per liter.\*\*

This solution contains sodium and chloride in the same relative proportions as exist in plasma (1.5:1) and is used in patients with severe acidosis to avoid the acidotic effects of isotonic saline.

#### 2. Hypotonic Multiple Electrolyte (Polyionic) Solutions

(a) Butler's solution (1950)<sup>3†</sup> containing in

\*Prepared by adding 150 cc. isotonic saline to 300 cc. of 5 per cent Dextrose in distilled water. This 450 cc. should be sufficient for the initial rehydration of most children.

\*\*Prepared by mixing 150 cc. isotonic saline and 300 cc. 5 per cent Dextrose in distilled water, and adding 12 cc. of molar sodium lactate. (Each cubic centimeter of molar sodium lactate contains 1 meq. of sodium.)

†Prepared by adding one ampule of Butler's solution (1950) and 10 cc. of 3 per cent magnesium chloride to 1000 cc. of 5 per cent Dextrose in distilled water.

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each liter: Sodium—55 meq., potassium—23 meq., chloride—45 meq., Lactate—26 m-moles, magnesium—5 meq., phosphate—12 m-moles, in 5 per cent dextrose and distilled water. (Electrolyte No. 2 in Travert® (Baxter) is similar to Butler's solution. However, 10 per cent invert sugar is employed in place of 5 per cent Dextrose).

(b)  $\frac{1}{3}$  Darrow's solution,  $\frac{2}{3}$  5 per cent Dextrose in distilled water, and 11 cc of 10 per cent potassium acetate per liter.<sup>‡</sup>

This solution will contain in each liter: sodium 41 meq., potassium 23 meq., and chloride 35 meq. (Darrow's solution is available under several trade names). This solution is used for infants whose renal immaturity might preclude phosphate administration. It may also be used as an alternative to Butler's solution in older children and adults.

These fluids can be satisfactorily used as the routine solutions in the treatment of patients requiring intravenous fluid therapy whether acidosis or alkalosis is present. There are, however, a few notable exceptions to their universal employment; adrenal insufficiency, where potassium containing solutions are contraindicated; severe hypotonic dehydration from any cause (i.e., adrenal insufficiency, prior subcutaneous treatment with hypotonic solutions, and heat prostration); unusually high gastrointestinal losses as in ulcerative colitis, where electrolyte losses are greater than can be replaced by hypotonic solutions; renal insufficiency; and in the immediate postoperative period where the amount of water and electrolytes must be greatly restricted.

The determination of the amount of fluid needed is facilitated by the use of a graph, such as Figure 1, which eliminates the usual steps in the calculation, and allows the fluid needed to be determined directly from the weight. For example, a baby weighing 10 kg (22 lbs.) who is moderately dehydrated will receive 1100 cc. of fluids in twenty-four hours ( $0.47 \text{ m}^2 \times 2400 \text{ cc.}$ ).

The initial hydrating solution of  $\frac{1}{3}$  isotonic saline may be given at a rapid rate for a short period of time to establish the adequacy of renal

<sup>‡</sup>Prepared by mixing 150 cc. Darrow's solution and 300 cc. 5 per cent Dextrose in distilled water, and adding 5 cc. of 10 per cent potassium acetate (each cc. of 10 per cent potassium acetate contains 1 meq. of potassium). If a large amount of solution is required, mix 500 cc. Darrow's solution and 1000 cc. 5 per cent Dextrose in distilled water, and add 17 cc. of 10 per cent potassium acetate.

function before the polyionic solution is started. It may be given at a rate of 8 cc/m<sup>2</sup>/minute for forty-five minutes following which, if the patient has not voided, the rate is decreased to 2 cc/m<sup>2</sup>/minute until voiding occurs.

If evidence of circulatory collapse is present or appears imminent, blood or plasma should be used at the beginning of therapy. Amounts of blood and plasma given are not included as a part of the total fluid to be administered.

After the dehydration and electrolyte deficits have been corrected, and if no continued extra losses occur, the rate of fluid administration may be decreased to a value nearer the maintenance volume of 1500 cc/m<sup>2</sup>/24 hrs. for the duration of the intravenous fluid therapy.

### Routes of Administration

Parenteral fluids are usually given either intravenously or subcutaneously. However, the use of subcutaneous fluids should be limited to short term therapy of non-dehydrated or slightly dehydrated children. The most serious consequence of dehydration is circulatory collapse, and only by placing the repair solution directly into the vascular compartment can the physician be certain that the fluids are immediately available to begin rehydration and prevent shock.

The absorption of subcutaneous fluids is too uncertain to depend upon when the patient is dehydrated. Patients treated by clysis will sometimes go into shock with enough fluid to have prevented the shock still pooled in the subcutaneous tissues.

If circulatory collapse is present or imminent when the patient is seen, intravenous therapy is mandatory, since blood or plasma must be given immediately to restore cardiac and renal function.

Subcutaneous fluids are suitable for a child with mild dehydration, if the abnormal loss of fluid has already stopped. The patient can often be sustained until he is able to tolerate oral fluids. Solutions given by clysis should have an electrolyte concentration isotonic with plasma. Hypotonic fluids may actually make the patient worse, at least temporarily, by drawing electrolytes from the plasma before the fluids can be absorbed. *None of the solutions listed above should be given subcutaneously.*

### Sites for Administering Intravenous Fluids

In small children or infants, the veins in the scalp are usually the most dependable. The hair

## FLUID AND ELECTROLYTE BALANCE—WORTHEN AND RAILE

must be shaved, and a small needle, either No. 22 or No. 23 should be used.

The veins on the dorsum of the hand can also be used, although in obese infants, the support for the vein may be so lax that difficulty is encountered in trying to insert the needle.

The saphenous vein as it courses anterior to the medial malleolus is an excellent site, because the position of the vein is quite constant. This vein can be entered in children of almost any age, even if it is not visible.

In older children, the antecubital veins are used most frequently, but the saphenous vein or the veins on the dorsum of the hand can be substituted if necessary.

If the child is in shock and a vein cannot be readily located, a cut-down may be done immediately. The saphenous vein is usually used. The incision is made just anterior and superior to the medial malleolus, and the polyethylene tubing is inserted through a small nick in the vein.

It should be emphasized that the daily intravenous fluid requirement should always be given over a twenty-four-hour period, rather than intermittently, to avoid the danger of overloading the vascular compartment.

### References

- Adolph, E. F., and others: *Physiology of Man in the Desert*. New York: Interscience Publishers, Inc., 1947.
- Astwood, E. B., Flynn, J. M., and Krayer, O.: Effect of continuous intravenous infusion of glucose in normal dogs. *J. Clin. Investigation*, 21:621, 1942.
- Butler, A. M.: Diabetic coma. *New England J. Med.*, 243:648, 1950.
- Butler, A. M., Talbot, N. B., Burnett, C. H., Stanbury, J. B., Mac Lachlan, E. A.: Metabolic studies in diabetic coma. *Tr. A. Am. Physicians*, 60:102, 1947.
- Butler, A. M., Talbot, N. B., Mac Lachlan, E. A., Appleton, J. E., and Linton, M. A.: Effect of testosterone propionate on losses incident to inadequate dietary intake. *J. Clin. Endocrinol.*, 5:327, 1945.
- Danowski, T. S., Austin, A. C., Gow, R. C., Maister, F. M., Weigand, F. A., Peters, J. H., and Greenman, L.: Electrolyte and nitrogen balance studies in infants following cessation of vomiting. *Pediat.*, 5:57, 1950.
- Darrow, D. C.: The retention of electrolyte during recovery from severe dehydration due to diarrhea. *J. Pediat.*, 28:515, 1946.
- Elkington, J. R., and Tarail, R.: Present status of potassium therapy. *Am. J. Med.*, 9:200, 1950.
- Flink, E. B., and Zimmerman, B.: Fluid and electrolyte balance: I. Basic considerations. *Minnesota Med.*, 37:545-557, 1954.
- Gamble, J. L.: Physiological information from studies on the life raft ration. *Harvey Lectures*, 1946-1947, pp. 247-273. Lancaster, Pa.: The Science Press Printing Company, 1947.
- Gamble, J. L., and Butler, A.: Measurement of renal water requirement. *Tr. A. Am. Physicians*, 58:157, 1944.
- Holt, L. E., Jr., and McIntosh, R.: *Holt Pediatrics*. 12th Ed. New York: Appleton-Century-Crafts, Inc., 1953.
- Lowe, C. U., Rourke, M., Mac Lachlan, E. A., and Butler, A. M.: Use of parenteral potassium therapy in surgical patients. *Pediat.*, 6:183, 1950.
- Newburgh, L. H., and Johnson, N. W.: The insensible loss of water. *Physiol. Rev.*, 22:1, 1942.
- Stewart, J. D., and Rourke, G. M.: Effects of large intravenous infusions on body fluid. *J. Clin. Investigation*, 21:197, 1942.
- Talbot, N. B., Crawford, J. D., and Butler, A. M.: Homeostatic limits to safe parenteral fluid therapy. *New England J. Med.*, 248:1100, 1953.

### FELLOWSHIPS IN HEART DISEASE RESEARCH

The Life Insurance Medical Research Fund announced in June, that it has this year awarded \$878,000 in grants and fellowships to be devoted to heart disease research.

This year's allocation includes \$734,000 as grants-in-aid for fifty-four research programs and \$144,000 to support thirty-eight fellowships for young men and women in training as research workers. Studies under these grants will be conducted in forty-seven institutions in twenty-four states, the District of Columbia, Canada and Denmark.

The grants will enable scientists to study the causes of heart failure, high blood pressure, surgery of the heart

and blood vessels, virus infections of the heart, hardening of the arteries, obesity, and other highly specialized basic research. As in the past, findings of these investigations will be reported in scientific journals for the widest possible distribution to other researchers and to physicians.

The Life Insurance Medical Research Fund, which receives contributions from more than 140 large and small U. S. and Canadian life insurance companies, is the pioneer agency supporting the scientific study of diseases of the heart and blood vessels. These diseases, now the nation's No. 1 health problem, cause over half of all deaths.

## NON-TUBERCULOUS CAVITIES IN THE LUNG

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IT IS MY purpose to review the causes and some of the perhaps not so well known signs, symptoms and diagnostic criteria of certain non-tuberculous cavities in the lung, with illustrations from a selected group of cases. At the outset I would like to emphasize one very important point, very valuable, I believe, for the general practitioner. For many years, it has been a good clinical rule that any patient with a fairly considerable amount of sputum negative for tubercle bacilli on many repeated examinations, especially if there was a cavity on x-ray examination, did not have pulmonary tuberculosis. This has been a good general rule but it has failed often enough to make it very necessary to be extremely cautious in the exclusion of tuberculosis as the cause of pulmonary cavity. This is all the more true today when chemotherapy may temporarily render the sputum negative.

I shall present instances of cavity formation in patients with Friedlander's bacillus pneumonia, coccidioidomycosis, actinomycosis, histoplasmosis, paragonimiasis, Hodgkin's Disease, cancer and tuberculosis masquerading as simple abscess of the lung.

### Friedlander's Bacillus Pneumonia

*Case 1.* A man, aged fifty-seven, hospitalized on September 5, 1951, was desperately ill with high fever, mental confusion, and sputum containing the Friedlander's bacillus (Fig. 1). Physical examination showed dullness and absence of breath sounds over the left upper lobe.

He was treated with streptomycin 4 gm daily for four weeks and then 2 gm daily for four more weeks. On November 8, 1951, the left upper lobe was removed because it had become an abscess.

*Comment.*—This Friedlander's bacillus (*Klebsiella pneumoniae* or *b. mucosus capsulatus*) is a non-motile, Gram-negative, non-spore-bearing organism. It is found in the respiratory passages in 2 to 25 per cent of normal persons and also in the intestinal tract of both infants and adults. It

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causes slightly over 1 per cent of clinical pneumonias. Jaffe<sup>7</sup> classified 198 Friedlander bacillus infections: 79 per cent were about equally divided between the genito-urinary tract, the gastrointestinal tract and the liver and bile tracts; 12½ per cent involved the lungs and the respiratory tract; 5 per cent the skin and appendages, and 3½ per cent the female internal genitalia and the vagina.

Pulmonary Friedlander infections may be divided into four groups: (1) acute, (2) chronic, (3) focal, and (4) septicemic. There is a marked predilection for the elderly, the alcoholic and the diabetic. The upper lobes were affected in 80 per cent of the cases where the lungs were involved and more than one lobe was involved in 30 per cent. An abscess develops in the lung in 60 per cent and an empyema in 23.4 per cent of the cases. Characteristically the thick viscous sputum blocks the bronchi and interferes with ventilation so that the breath sounds over the involved areas are suppressed. Persistent thin-walled cavities with metastatic lesions elsewhere in the lungs simulates chronic pulmonary tuberculosis but the sputum is consistently negative for tubercle bacilli. Blood cultures are positive in more than half the cases of Friedlander's bacillus pneumonia.

The course of the disease roughly may be divided into two stages: first, the acute stage in which death may come quickly; the second, resembling very closely pulmonary tuberculosis with chronic course due to varying amounts of pulmonary fibrosis, suppurative pneumonitis, cavitation, bronchiectasis and perhaps empyema. One-sixth of the patients with pulmonary involvement recover satisfactorily; two-sixths develop chronic suppurative pneumonitis; three-sixths die.

### Coccidioidomycosis

*Case 2* is presented because it illustrates the persistence of the organism, *coccidioides immitis*, in the body after approximately eight years without symptoms. This patient has shown no pulmonary involvement at any time. Figure 2, of another patient, shows a typical residual cavity from primary coccidioidomycosis. While a soli-

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tary thin-walled cavity with little reaction around it is characteristic and highly suggestive of a cyst, multiple coccidioidal cavities do occur and the cavities are by no means all thin-walled.

*mitis* was recovered in pure culture many times from these abscesses. At no time have X-rays of the chest shown any lung or mediastinal glandular involvement.

He was in Colorado General Hospital about one year;

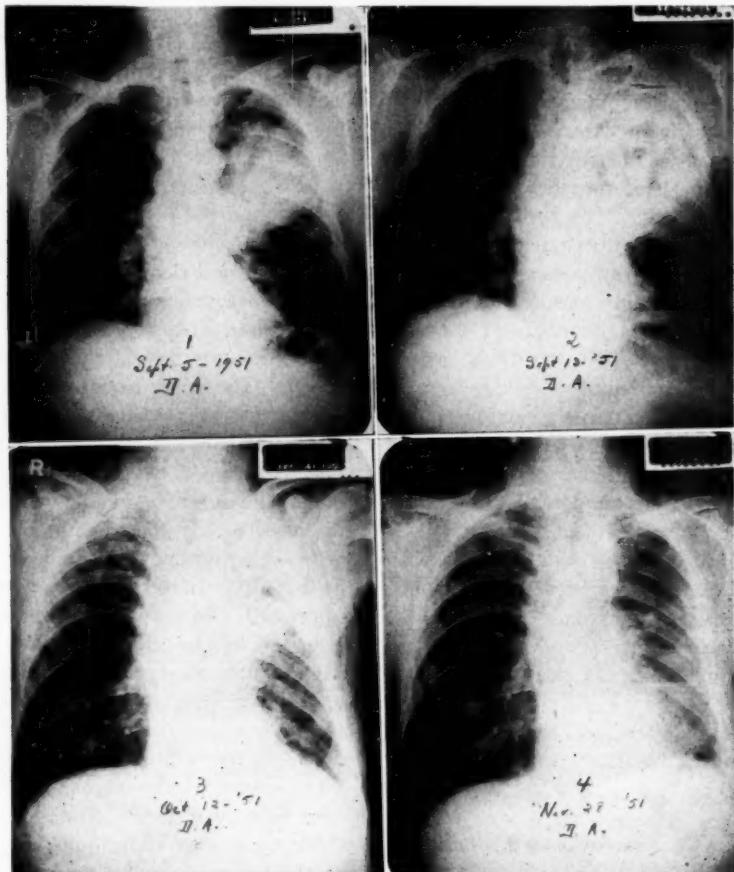


Fig. 1. Friedlander's bacillus pneumonia, abscess left upper lobe. Man aged fifty-seven years.

*Case 2.* E. W., a white man, aged fifty-six in 1953. In the early fall of 1940, two and a half months after arrival in California where he worked in the San Joaquin Valley, he became ill with what his doctors called "Valley Fever." He stayed in bed at home two weeks. One week after returning to work, he developed an abscess on the middle finger of his left hand and had to quit work. He returned to Colorado.

He was admitted to Colorado General hospital, April, 1941, with six abscesses, and bone involvement of the left middle finger, right olecranon, right acromion process and sternum; one abscess of the left hip with involvement of the ischium, one abscess of the left groin and one soft tissue abscess of the left forearm. During the following year he had many other soft tissue abscesses without additional bone involvement. *C. im-*

was treated with increasing doses of coccidioidin at first subcutaneously and later intravenously and made a remarkable recovery.

He resumed regular work in January, 1945, and has since been well until October, 1952, when he bruised the skin on the right elbow. A sore developed from which *C. immitis* was recovered in pure culture. This healed in a few weeks and no further symptoms have developed.

*Comment.*—Coccidioidomycosis is a fungus infection resembling closely in many ways pulmonary tuberculosis. The primary form of the disease is an acute, benign, self-limited respiratory infection. According to Winn,<sup>10</sup> in this primary stage pleural pain may be extremely severe

## NON-TUBERCULOUS CAVITIES IN THE LUNG—WARING

suggesting occasionally a coronary occlusion, gall stones or renal colic or a broken rib. The headache sometimes is very severe and may suggest the headache of acute poliomyelitis or tumor of the brain. Toxic erythemas resemble measles and scarlet fever. The pain in the joints and in the limbs may suggest acute rheumatic fever. The typical rashes of erythema multiforme or erythema nodosum are highly suggestive, especially when they occur in recent visitors to the endemic area of California. The erythema nodosum may be used as an index of the incidence of the disease. Five per cent of newly arrived persons in the endemic area who become infected and about 20 per cent of the patients who have proven coccidioidomycosis develop erythema nodosum.

The secondary stage of the disease, coccidioidal granuloma, is a chronic, progressive, disseminated disease with a 50 per cent mortality. When dissemination takes place it is almost always early in about 1 per cent of patients clinically diagnosed with this infection and in about one in 500 of all those infected. During the first week of the infection 50 per cent of the cases have a positive precipitin test, 15 per cent have a positive skin test and only 10 per cent have a positive complement fixation test. Cases with erythema nodosum react very strongly to the skin test. No case of fatal dissemination has been reported from the residual cavity. Smith<sup>15</sup> says: "None of our military coccidioidal patients, of whom we had records of thousands, has ever been reported to us as having undergone a post-war dissemination."

A cavity may develop after completely inapparent infection. Few cavities produce sufficient symptoms to warrant the patient seeking medical advice. The most common symptom of cavity is hemoptysis. A cavity may appear transiently during the acute infection and then disappear or one may develop months after the acute infection is over and thus be missed. For these reasons the true incidence of cavity is difficult to determine.

Criteria for proof of coccidioidal nature of cavity: (1) recovery of fungus, (2) positive serology, precipitins during acute phase and complete fixation of complement in at least first 1:2 dilution of serum, (3) a positive coccidioidin skin test with a negative tuberculin test.

A small number of double infections, coccidioidomycosis and tuberculosis, are recorded. Coccidioidomycosis rarely activates quiescent tuberculosis. Tuberculous patients hospitalized in

endemic areas have acquired coccidioidomycosis from the ever-present dust containing chlamydospores (Smith).<sup>15</sup>

The pulmonary segment or lobe most frequently

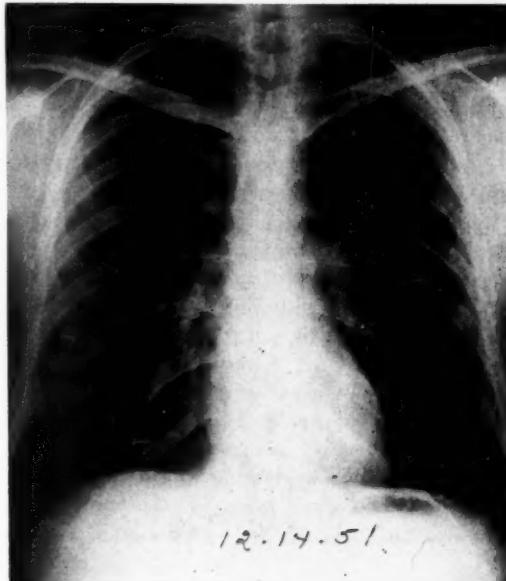


Fig. 2. Coccidioidomycosis. Residual cavity.

involved with a primary coccidioidal cavity is not known since many cases have not had special x-ray examinations to identify accurately affected lobes. Roughly, in the films 70 per cent of the cavities are in the upper lung fields and 30 per cent in the lower. Spontaneous hydro-pneumothorax during the initial infection even without demonstration of cavity has been reported. In recording the history of the patient, residence two to three months preceding onset of symptoms should be carefully noted. Since 25 per cent of cavity cases may be serologically negative and the skin test give only "a faint blush," a positive diagnosis can be made only by recovery of the fungus. The sedimentation rate may be normal in 75 per cent of coccidioidal cavity cases but, in contrast, it is infrequently normal in tuberculous cavity cases. Surgical procedures on the lung do not stir up the infection even to the extent of increasing the titer of the complement fixation reaction. As in tuberculosis, terminal cases of histoplasmosis, coccidioidomycosis and blastomycosis may become anergic and give negative skin tests, but the complement fixation test rises in these cases (Smith).<sup>16</sup> Only patients with excessive sensitiv-

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ity to coccidioidin, positive reactions to 1:10,000 dilution, show cross reactions with histoplasmin or blastomycin. Persons with marked reactions to histoplasmin may give cross reactions with blastomycin.

Winn<sup>19</sup> in a study of ninety-two coccidioidal cavities says 25 per cent closed spontaneously, 10 per cent persisted without further complications and 5 per cent filled and became "solid" lesions radiologically. The balance required surgery.

Racial predilection in this disease is so conspicuous that it is worthwhile recording: Dissemination occurs in one in 500 infected Caucasians, three and one-half times as frequently in Mexicans, fourteen times as frequently in Negroes and 180 times as frequently in Filipinos (Jillson).<sup>8</sup>

There is no evidence of person to person transmission. The return to normal of the "sed rate" is a dependable clinical sign of cure.

The coccidioidin skin test is a valuable and at the same time a very safe test. It differs from the tuberculin test in certain important particulars. Its virtues and significance may be summarized as follows:

1. It does not sensitize.
2. Unlike tuberculin, it does not cause focal reactions.
3. Unlike tuberculin, it does not stir up quiescent lesions.
4. It does not interfere with serologic tests.
5. As with the tuberculin test, conversion of the coccidioidin test from negative to positive is highly significant. In doing the tests one must carefully avoid using tuberculin contaminated syringes. Syringes used for tuberculin tests should be reserved solely for that purpose!
6. The tuberculin test is helpful in differential diagnosis.
7. Simultaneous skin tests should be done for blastomycosis, histoplasmosis and coccidioidomycosis; if all react positively, the strongest test is the significant one.
8. After primary infection there is remarkably solid immunity to exogenous reinfection. The acquired immunity after naturally acquired primary infection with tuberculosis or BCG vaccination is only relative.

Indications for surgery in coccidioidomycosis include: (1) a giant cavity, a block cavity or an infected cavity, (2) rupture of a cavity into the

pleural space with pneumothorax or empyema, (3) an unexpanded lung after rupture, (4) repeated severe hemoptysis, (5) formation of a coccidioma, (6) some surgeons recommend that all residuals should be removed surgically regardless of activity. J. A. Weinberg advises delaying surgery if the complement fixation test is high.

We are so disappointingly aware of the great tendency of primary tuberculosis to progress or to become latent and later to relapse that it is hard to appreciate the solid immunity conferred by uncomplicated primary coccidioidomycosis. All clinical experience is against exacerbation or late dissemination from residual lesions. However, it is still remotely possible that dissemination *may* take place from a primary focus since: (1) patients have been observed with coccidioidal meningitis and an associated old localized lesion, (2) patients dead of disseminated coccidioidomycosis may have fresh lesions and also older localized lesions, (3) lymph node, bronchial or blood vessel ulceration furnish the opportunity for lymphogenous, bronchogenic or hematogenous spread, (4) organisms remain viable and can be cultured from these early lesions even after fifteen years, (5) Puckett<sup>11</sup> has found the mycelial form in a majority of resected coccidioidal lesions both solid and cavity, (6) Forbus<sup>3a</sup> says as long as the primary lesion remains, the danger of dissemination is possible. Winn<sup>19</sup> has never seen a fatal dissemination from a residual pulmonary cavity. It should be emphasized again that early infection and subsidence of this early infection evidently produces a strong immunity both to exogenous reinfection and to endogenous exacerbation and dissemination.

Craddock<sup>3</sup> has itemized the general features of the mycoses and some associated conditions as follows (with modifications and additions):

1. Calcification of pulmonary lesions is common in tuberculosis, coccidioidomycosis, and histoplasmosis.
2. Cavity formation is common in tuberculosis, coccidioidomycosis and actinomycosis and infrequent in histoplasmosis.
3. Mediastinal glandular involvement is common in tuberculosis; in 16 per cent to 65 per cent of the cases of coccidioidomycosis; in actinomycosis and blastomycosis and histoplasmosis and, incidentally and conspicuously, in sarcoidosis.
4. Central nervous system involvement is par-

## NON-TUBERCULOUS CAVITIES IN THE LUNG—WARING

ticularly important and frequent in tuberculosis, torulosis, actinomycosis and nocardiosis and histoplasmosis.

5. Blastomycosis is prone to involve the skin, the lungs, the bones. It also should be noted that cases are appearing secondary to antibiotic chemotherapy.

6. Histoplasmosis may involve the mucous membranes anywhere, the mouth, the gastrointestinal tract. It also may involve the lungs, the adrenals, the central nervous system. Histoplasmosis is now recorded as one of the causes of Addison's Disease. It should be noted that histoplasmosis occasionally complicates or is complicated by tuberculosis, diabetes, leukemia or lymphoblastoma.

"Round lesions" discovered by the x-ray are found in about 2 per cent of persons in mass surveys. These round lesions may be divided as follows: tuberculomas 45 per cent; asymptomatic cancer of the lung 30 per cent; benign tumors 15 per cent; miscellaneous inflammatory lesions including mycoses 10 per cent.

### Histoplasmosis

Space does not permit many illustrations so I omit an illustration of cavity formation in histoplasmosis. In any case, it would look almost like chronic fibro-cavitory pulmonary tuberculosis. I include a brief discussion of histoplasmosis, since Furcolow<sup>4</sup> and others have reported the occasional confusion of this fungus disease with tuberculosis. This confusion is not surprising since histoplasmosis (1) may produce a chronic pulmonary disease with cavity formation, (2) sometimes appears under both epidemic and non-epidemic conditions as a widespread miliary pulmonary disease resembling miliary tuberculosis, (3) not infrequently involves the larynx and has been erroneously diagnosed tuberculosis, sarcoidosis or coccidioidomycosis, (4) may involve the adrenals and produce the clinical picture of Addison's Disease, (5) shows calcification of old lesions and, (6) finally, may complicate tuberculosis.

In a valuable paper, Israel<sup>6</sup> described four principal types: (1) active primary histoplasmosis, (2) healed primary, (3) active disseminated and (4) chronic disseminated. Jillson<sup>8</sup> suggests a convenient classification: I. Pulmonary, both symptomatic and asymptomatic (non-epidemic and epidemic forms); II. Disseminated (non-fatal and fatal); and III. Localized (skin,

penis, tongue and larynx). Furcolow and Grayston<sup>4</sup> have collected 116 cases of the epidemic form in a retrospective study of eleven epidemics. A strikingly consistent symptom complex accompanied the illness in all the epidemics. The x-ray typically showed numerous widely disseminated discrete infiltrations varying in size from small, finely granular lesions through snowflake appearance to discrete nodules. A high percentage eventually healed with miliary calcification.

Clinically, histoplasmosis usually begins with lesions in the mouth or the lungs. *Cavitation is uncommon.* Half of the reported cases were diagnosed at post mortem. The organisms have been isolated from 50 per cent of the cases. In fatal cases the gastrointestinal tract is almost always involved. Up to 1950 there were 123 cases reported in the literature and the lungs were involved in sixty-two. Up to August of 1952, 178 cases have been reported in the literature, and the proportion of those with lungs involved remains the same, at about 50 per cent. Cultures of the organisms in the sick patient are usually fairly reliable. Of 138 cases reported up to January, 1950, 20 per cent were in infants. Other diseases are not infrequently associated with or complicated by histoplasmosis infection. For instance, of 123 cases, concomitant tuberculosis was found in thirteen, Addison's Disease in six, Hodgkin's Disease or other lymphoblastomas in four, leukemia in two, diabetes in three, erysipelas in three. The incidence of concomitant malignant lymphomas (chiefly Hodgkin's Disease) in cryptococcosis and disseminated histoplasmosis is about 10 per cent (Jillson).<sup>8</sup>

The tuberculin test may become negative with the onset of Hodgkin's Disease and a similar depression of the serologic reactions for syphilis has been noted. It may be surmised that the malignant lymphomas predispose to cryptococcosis and histoplasmosis by alterations in the host's resistance.

Note that this disease, histoplasmosis, heavily involves the reticuloendothelial system, with a marked frequency of involvement of the orifices of the body, the gastrointestinal tract, the adrenals, the lungs and the lymph nodes and the central nervous system. Schulz reported involvement of the central nervous system in twelve of 120 cases. There is no evidence of person to person communication but dog to dog transmission is reported. Bone marrow cultures are some-

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times helpful in detecting the organism. Mice should be injected intraperitoneally with the proper material. After three to six weeks the mouse is killed and the spleen and liver are

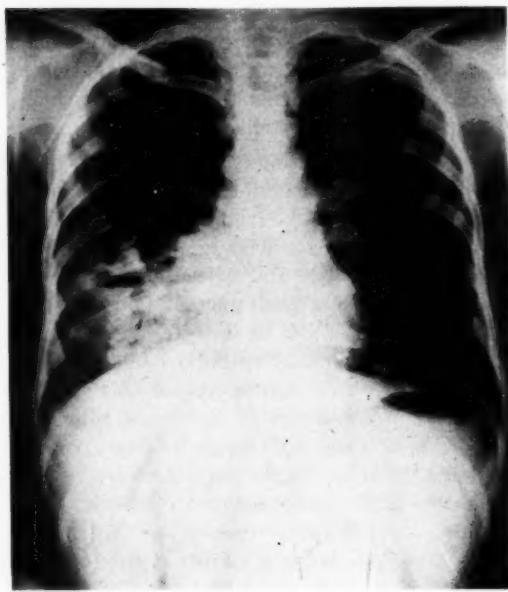


Fig. 3. Paragonimiasis. Cavity right lower lobe.

streaked on media suitable for the growth of fungi. Puckett<sup>12</sup> has found the Periodic-Acid-Schiff Stain very valuable in identification of the organisms in resected lung lesions.

Christie<sup>2</sup> records his observations on the treatment of twelve cases of histoplasmosis with a fatal prognosis. These cases were treated with a preparation called ethyl-vanillate. This preparation is used orally as a 40 per cent solution in olive oil; dose given 0.5 gram every five to six days until 1.5 gram per kg. body weight per day is attained. Of twelve cases with fatal prognosis, five recovered and are alive and well after the use of this drug ethyl-vanillate.

### Paragonimiasis

From the material of Roque, Ludwick and Bell,<sup>13</sup> Figure 3 shows a radiograph of an American soldier returned from Korea demonstrating a pulmonary cavity due to paragonimiasis. Since this patient had the highly suggestive combination of hemoptysis and a cavity in the lung, it is not surprising that it was originally thought that he had pulmonary tuberculosis. Because it is prob-

able that pulmonary paragonimiasis will be seen, though rarely, among our American soldiers returned from Korea, it is important that we know of the existence of this disease and be on the alert not to confuse it with tuberculosis.

Paragonimiasis is called *endemic hemoptysis*. *Schistosomiasis* is *endemic hematuria*. Pathogenesis: Ingestion of a crab in the endemic area results in the liberation of the fluke from the cyst. The fluke migrates through the diaphragm and matures in cysts and in tunnels in the lungs. Diagnosis is dependent upon five criteria: (1) residence in the endemic area in Korea or Japan, (2) generally good condition of the patient, (3) a story of chronic or intermittent hemoptysis, (4) an x-ray showing lesions in the lungs, (5) the demonstration of the typical ova in wet preparations of the sputum or in some other tissue. The ovum is operculated (has a lid) and resembles the ovum of the fish tapeworm.

Important clinical causes of hemoptysis that the general practitioner should bear constantly in mind these days are: (1) tuberculosis, (2) bronchiectasis, (3) mitral stenosis, (4) infarction, (5) abscess of the lung, either simple or cancerous, (6) fungus infections of the lung, (7) paragonimiasis.

### Actinomycosis

The vast majority of fungus infections of the lungs are caused by coccidioidomycosis, histoplasmosis and actinomycosis. "Valley Fever" and coccidioidal granuloma, as has been pointed out, represent only a very small part of those infected with *coccidioides immitis*. Cases of clinical histoplasmosis are being recognized more frequently but their absolute number is still small, and again inapparent infections, cases recognized only by a positive histoplasmin test and/or serologic tests, with or without few or many calcified pulmonary lesions, far outnumber those with manifest active disease. These inapparent infections of coccidioidomycosis and histoplasmosis have been identified by serologic reaction and skin tests. The situation with actinomycosis is different. Attempts to devise serologic reactions and skin tests have been unsuccessful. *Coccidioides immitis* and *histoplasma capsulatum* are widely distributed in nature, the former in endemic areas in California, Arizona and Texas, the latter mainly but not exclusively in the Mississippi Valley. Perhaps, because "lumpy jaw" of cattle was a common, as

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well as the first recognized, form of actinomycosis, it was originally thought (Bostroem, 1891) that actinomycosis results from traumatization with grass or straw carrying the infective agent and, therefore, the rural incidence must be greater than urban. Today we know better. The true

general application. The number of inapparent actinomycotic infections is therefore conjectural, but must be comparatively few.

*Case 3.* R. G., a single Spanish-American girl, aged twenty-three, entered the hospital February 25, 1946, in a comatose state with high fever, frequent cough with

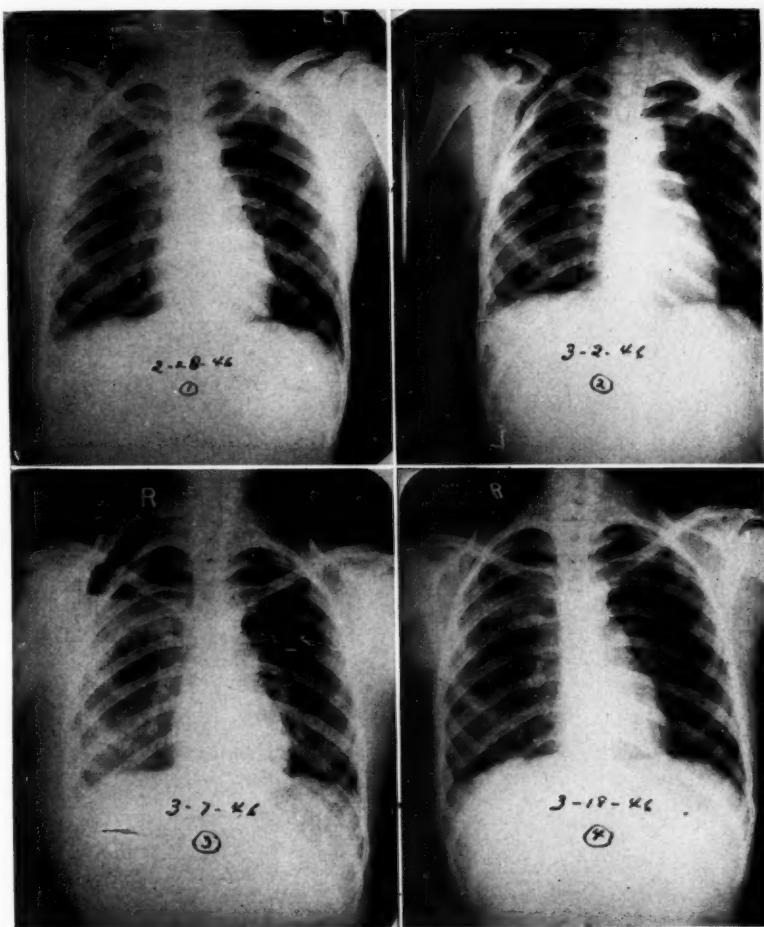


Fig. 4. Actinomycosis. Abscess left lung with broncho-pleuro-cutaneous fistula and large abscess chest wall. Note subcutaneous emphysema No. 2 and No. 3 and fluid level No. 3.

actinomycetes has not been found in nature "apart from a parasitic habitat," but is commonly present on human tooth surfaces, in the tartar on teeth, in tonsillar crypts and perhaps on mucous membranes. Aerobic actinomycetes (Genus *nocardia*) is found in nature. Though Glover et al. have reported an instance of sensitivity to a suitable antigen of *N. asteroides* in human infection, reliable skin and serologic tests have not received

bloody sputum, a tremendous fluctuating and crepitating abscess under the soft tissues of the back extending from the shoulder to the buttock, and abscesses on the left wrist and right elbow; bloody diarrhea and urinary incontinence.

On March 8, 1200 cc of pus were evacuated from the abscesses and *A. bovis* successfully cultured from this material. The patient was treated with large doses of penicillin and sulfadiazine and made a dramatic improvement. Note the subcutaneous emphysema in films 1, 2 and 3 and the fluid level extending beyond the chest wall

## NON-TUBERCULOUS CAVITIES IN THE LUNG—WARING

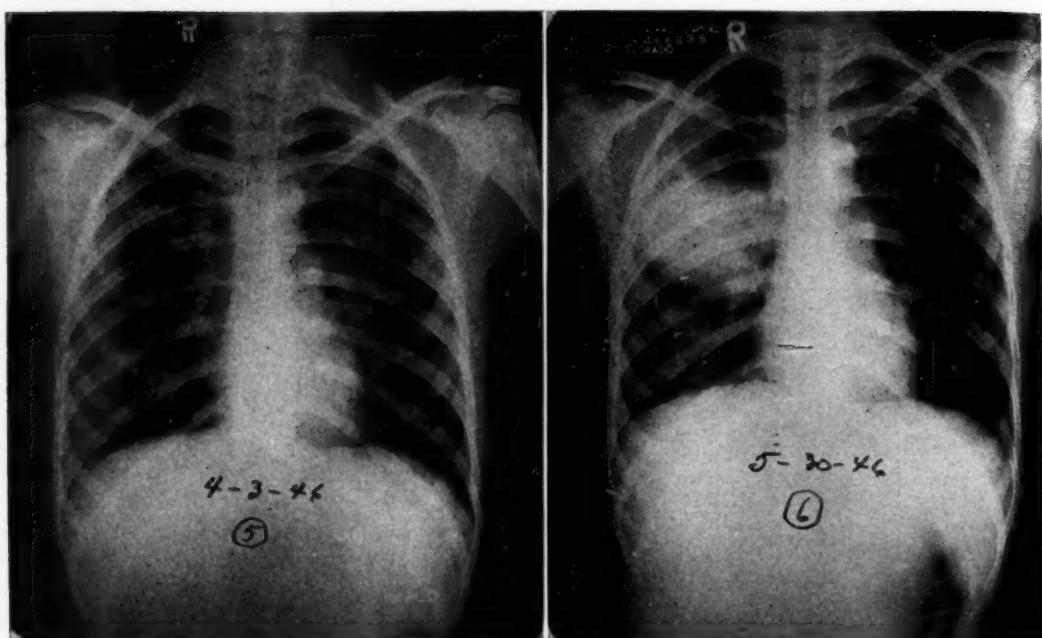


Fig. 5. Actinomycosis. Same case, showing improvement No. 5 and abscess No. 6 after hemorrhage.

in film No. 3, dated March 7, 1946, before surgery (Figs. 4 and 5).

She was so much improved by April 11, 1946, that, unwise, I let her return home, under injunction, however, to continue the penicillin and sulfadiazine. She shortly began to hemorrhage very severely, returned to us, and despite prompt surgery, died on August 16, 1946. It would have been much wiser to have done a lobectomy before letting her return home.

**Comment.**—A classification of the clinical cases of actinomycosis shows that: (1) cervico-facial, 56.8 per cent, (2) abdominal 22.3 per cent, (3) thoracic, 15 per cent, (4) elsewhere, 5.9 per cent. Note that the tongue is involved in 3 per cent of the cases. Pathogenesis: The disease originates (1) from the mouth by aspiration of infected material from around the teeth and gums (2) by extension of the disease up through the diaphragm into the lungs and (3) from metastasis. Characteristic pathology of the disease includes sinus formation and scar formation, all being of chronic nature.

Actinomycosis may be classified mainly from a clinical standpoint into two groups: Infections due to the anaerobic organism *a. bovis* which is Gram positive and is the agent in 90 per cent of the clinical infections of actinomycosis, and infections due to the aerobic organism called *nocard-*

*dia asteroides* which is a partly acid-fast organism pathogenic for animals. Ordinary methods of concentration of sputum interfere with the growth of this nocardia organism. Neither form is communicable from person to person.

Kirby and McNaught<sup>9</sup> reported two cases of nocardiosis. Reviewing the literature they collected thirty-four cases of which the lungs were involved in twenty-five; the brain was involved in eleven; the diagnosis was made at post mortem in twenty-one; and thirty of the thirty-four patients died. The organism causes a necro-suppurative segmental pneumonitis with numerous small abscesses. Fortunately, some of the newer broad spectrum antibiotics are proving helpful. Formerly the main remedies consisted of potassium iodide and the combined use of penicillin and sulfadiazine. McVay and Sprunt<sup>10</sup> reported seven cases of actinomycosis treated successfully with aureomycin intravenously. It should be added that irradiation may be helpful for superficial lesions and surgery may be helpful for some of the local lesions.

McLean reported on the successful treatment of seven cases of oro-cervical actinomycosis with terramycin. They gave 750 to 2000 mg daily for fourteen to forty-two days, for an average total dose of 46 gm in an average period of twenty-

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four days. They said they saw no severe toxic reactions.

In the *J.A.M.A.* for May 9, 1953, there is a report on the treatment of another fungus disease, blastomycosis, with a preparation called stilbamidine. The first day 50 mg were given in 10 cc of 5 per cent dextrose. From the third to the twenty-ninth day 150 mg were given daily in 500 cc of dextrose solution. Also the patient at this time was put on a low protein and low purine diet. David Smith says stilbamidine is first choice in the treatment of pulmonary and systemic blastomycosis regardless of the immunological status of the patient. This drug is not harmless and must be used with caution. In a fairly high percentage of patients the drug selectively damages the sensory root of the fifth nerve.\*

### Hodgkin's Disease

*Case 4.* M. R., a woman, aged forty-three, suffered onset of the disease in 1946 with severe generalized pruritus. Diagnosis of Hodgkin's Disease by axillary node biopsy was made in September, 1947; four courses of irradiation therapy and three courses of nitrogen mustard; continuous fever, right pleural effusion, many thoracenteses; forty-three pound weight loss in the past year; non-productive cough. X-ray: enlarged mediastinal nodes and widespread parenchymal involvement both lungs with cavity right lower lobe (Fig. 6). Sputum negative for acid fast bacilli. Death, October 31, 1950. Anatomical diagnosis: Generalized Hodgkin's Disease. Cavity right lower lobe, hydrothorax. No pathologic evidence of tuberculosis was found.

The lungs are involved in 15 to 40 per cent of all cases of Hodgkin's Disease. Pleural effusion is not infrequent. Granulomatous changes and thickening of the bronchial wall may lead to stenosis of the bronchus and obstructive pneumonitis which may suggest cancer, pneumonia or tuberculosis with cavity formation. Much later, nodules throughout the lungs may suggest metastasis from some malignancy originating outside the chest. Enlarged mediastinal nodes so commonly seen may suggest tuberculosis, lymphoma, erythema nodosum and sarcoidosis. Higginson

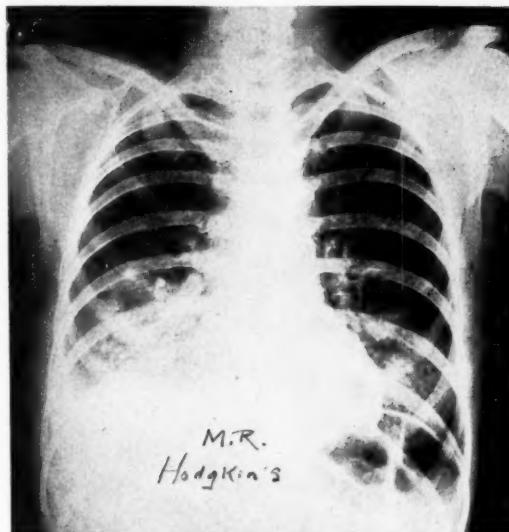


Fig. 6. Hodgkin's disease with cavity.

and Grismer<sup>5</sup> reported a biopsy proven case of Hodgkin's Disease with a pedunculated endobronchial tumor.

*Tuberculosis and Hodgkin's Disease.*—Wallhauser<sup>18</sup> collected from the literature the post-mortem reports of 151 cases of Hodgkin's Disease. Active or healed tuberculosis was found in thirty-one or 20 per cent of those 151 cases. Clinically active tuberculosis was found in twelve or 4.5 per cent of 267 cases. Healed or active tuberculosis was found at post-mortem in other forms of lymphoma in 5.3 per cent; in cases of cancer in 14.6 per cent; at general post-mortem examination in 19.3 per cent; and in patients with Hodgkin's Disease 33.3 per cent. In Hodgkin's Disease the tuberculin test is frequently negative in the presence of a complicating tuberculosis. However, a strongly positive tuberculin test is good evidence of tuberculosis. The tuberculin test may become positive after effective x-ray treatment has been given.

Because I believe that one understands a disease best if he knows something of the history of the development of our present knowledge of it, or even our deficient knowledge, I summarize here some landmarks which reveal, if nothing more, the baffling nature of this disease.

1. In 1832, Thomas Hodgkin confused the disease with tuberculosis.
2. In 1926, Fox re-examined some of the tis-

\*In a recent report, Snapper and McVay call attention to three mistaken notions about blastomycosis. Briefly, (1) this disease is not such a rarity that it need not be considered seriously in differential diagnosis, (2) laboratory procedures for diagnosis are neither difficult nor expensive and, finally, (3) the prognosis is by no means hopeless since new drugs are available. They note the toxicity of stilbamidine and recommend the use of 2-hydroxystilbamidine which they found of therapeutic value and without toxic sequelae. (Snapper, I. and McVay, L. V., Jr.: *Am. J. Med.*, 15:603 (Nov.), 1953.)

## NON-TUBERCULOUS CAVITIES IN THE LUNG—WARING



Fig. 7. Cavernous metastasis from seminoma of the testis.

sues from Hodgkin's original cases and found definite evidence of tuberculosis in some of them.

3. In 1898, Sternberg said that Hodgkin's Disease was a peculiar form of tuberculosis.

4. In 1928, James Ewing, in a memorable sentence dramatically emphasized the frequent association of these two diseases: "In New York where Hodgkin's Disease is common, tuberculosis follows Hodgkin's Disease like a shadow."

5. In 1931, L'Esperance said the disease was due to an avian tubercle bacillus.

6. In 1910, Fraenkel and Much found acid-fast rods in tissues of patients with Hodgkin's Disease.

7. In 1933, Wallhauser said that Sternberg had recently reaffirmed his theory that the cause of Hodgkin's Disease was tuberculosis.

8. In Hodgkin's Disease a factor is present not found in normal or cancer tissue which can be passed serially in fertile chicken eggs. The amniotic fluid from the eggs can interfere with the growth of the influenza virus in eggs.

### Carcinomatous Abscess of the Lung

Abscess of the lung is found most frequently in association with primary carcinoma of the lung, especially those forms leading to bronchial obstruction and consequent suppurative pneumonitis. Rarely, a metastatic carcinoma of the lung may break down and form a cavity. Brock<sup>1</sup> says a cancerous cavity may be caused by necrosis of the

primary growth itself, or it may arise in the obstructed and infected portion of the lung distal to the growth, or it may result from bronchial embolism or spill-over from the infected primary growth.

From the material of Salzman, Reid and Ogura,<sup>14</sup> the x-rays in Figure 7 illustrate the more rare condition: cavernous metastatic carcinoma of the lung. This is the picture of the lung of a man with pulmonary metastasis from seminoma of the testis. One year after removal of the testicular tumor, his chest film showed many solid and cavernous lesions in the lungs. Terminally, rupture of one of the cavities into the pleural space caused spontaneous pneumothorax. Five cases of spontaneous pneumothorax associated with metastatic carcinoma have been reported. According to Salzman et al., rapid growth of the metastatic pulmonary lesions with central necrosis, combined with infection and bronchial erosion, seem to be important factors in the pathogenesis of cavernous pulmonary metastatic carcinoma.

*Abscess of the Lung due to Primary Cancer.*—Strang and Simpson,<sup>17</sup> between 1946 and 1951 collected seventy cases of cancerous abscess of the lung from a British chest clinic. These cases were selected from a total of 1930 cases of bronchial carcinoma. Cancerous cavity was found in 3.6 per cent of 1930 cases of bronchial carcinoma. Cancerous cavity is found at post mortem in 12 per cent to 25 per cent of cases of cancer of the lung. According to Brock,<sup>1</sup> bronchial carcinoma was the cause of abscess of the lung in 13.8 per cent of 405 cases of lung abscess.

Of the seventy cases of cancerous lung abscess reported by Strang and Simpson, sixty-seven were in men and 70 per cent of the entire group were between the ages of fifty and sixty-five years. Squamous cell carcinoma was the most common cancer to cause cancer abscess of the lung; 30 per cent of forty cases of squamous cell carcinoma of the lung had abscess of the lung; 70 per cent of twenty-two cases of cancer with abscess were squamous cell carcinomas. Note that cancer of the middle lobe and, therefore, cancerous abscess of the middle lobe are rare. Sixty-three per cent of cancerous abscesses of the lung were in the upper lobes. Finally, one-third of lung abscesses in persons over forty-five years of age are due to cancer. Of Brock's

## NON-TUBERCULOUS CAVITIES IN THE LUNG—WARING

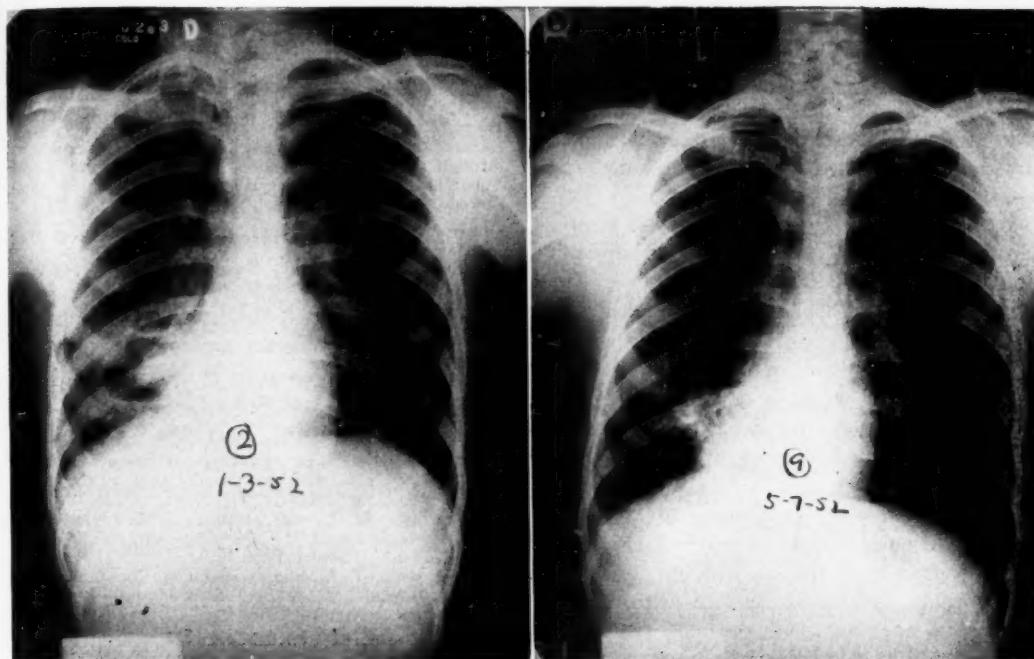


Fig. 8. Basal tuberculous cavity simulating non-tuberculous abscess of the lung.

eighty-three patients with abscess of the lung due to cancer, only four were in women, the other seventy-nine were in men. Therefore, age and sex are important influences. Eccentric cavitation is highly suggestive and rib erosion diagnostic.

### Basal Tuberculous Cavity

Finally, a case is reported of a tuberculous cavity (Figure 8) in the lower lobe of the right lung masquerading as a non-tuberculous abscess of the lung.

*Case 5.*—R. J., an eighteen-year-old Spanish-American boy, entered the hospital's surgical service, December 28, 1951 with chief complaint of twenty-five pound loss in weight in the preceding year, increasingly productive cough and fatigability and pain in the right chest anteriorly. Since his pre-admission diagnosis was non-tuberculous abscess of the lung and since the "abscess" was in the lower lobe and the rest of the lung on both sides was apparently clear radiologically, he was forthwith bronchoscopyed by an enterprising surgical resident without waiting for further sputum examination, which the next day, to the consternation of the bronchoscopist, showed innumerable tubercle bacilli.

*Comment.*—Tuberculous Cavity vs. Simple Abscess of the Lung: Several lessons can be drawn from this case. First, do not be too quick to ac-

cept the other fellow's diagnosis; second, if time permits, and it usually does, always examine the sputum carefully before bronchoscopy; third, since tuberculosis is ubiquitous and often unpredictable, all bronchoscopies should be done with as much care as if tuberculosis was already proven; fourth, tuberculous cavities do occur in the lower lobes and tuberculosis can be present even if repeated sputum examinations have been negative.

### Conclusions

In general, in trying to make an etiologic diagnosis of cavity in the lung, the following should be borne in mind:

1. Record the presence or absence of putrid odor to sputum and the presence or absence of putrid odor during bronchoscopic examination. This means a putrid abscess.
2. Record presence or absence of dentures and "oral sepsis," e.g., pyorrhea. Although one must without fail inquire carefully for a history of aspiration of a "*foreign body*," such history is relatively rare. Brock records only three foreign body abscesses in his 235 cases of abscess of the lung. Adults with upper dentures and children

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are the most frequent "victims." Aspiration of *foreign material* notably vomitus at any time and infected material from bad teeth and gums during dental extraction or other oral surgery, are much more frequent causes of aspiration pneumonia and simple and putrid abscess of the lung. (See No. 6 below).

3. The early correction of oral sepsis in pregnant women and the correction of oral sepsis before any elective operation are desirable. Thus can one best avoid aspiration pneumonitis.

4. Record presence or absence of thrombo-phlebitis in legs. Bland or septic pulmonary infarction may lead to cavity formation.

5. Record presence or absence of heart murmurs. Mural thrombi dispose towards pulmonary infarction.

6. Record presence or absence in history of loss of consciousness including particularly injury, especially fracture of the jaw with bleeding (traffic accidents), operative procedures with or without general anesthesia, intoxications (morphine, barbiturates, alcohol, diabetic coma, carbon monoxide, illuminating gas, et cetera), epilepsy, immersions, labor and delivery with or without vomiting, foreign body aspiration, prolonged use of oil, sprays or laxative oils. With any of these, aspiration pneumonitis can easily occur.

7. The advisability of gastric lavage before emergency operative procedures and the necessity of prompt bronchoscopic aspiration of any person vomiting during anesthesia should be considered.

8. Cavities behind the heart or in the vertebral gutter may be and often are missed because they are unsuspected and lateral and oblique films of chest are not made. Precise lobar localization of cavities is helpful in diagnosis, e.g., a cavity in the middle lobe is not likely to be cancerous, but is much more likely tuberculous since the middle lobe bronchus is peculiarly vulnerable to compression from tuberculous glands as part of a primary complex. Tuberculous cavities are most apt to be found in the apical and posterior segments of the upper lobes and the superior segment of the lower lobes. Posture of the patient at time of aspiration plays an important part in determining where aspirated material will lodge. *Tomograms often reveal unsuspected cavities.*

9. Record residence or not in endemic areas for Coccidioidomycosis and Histoplasmosis.

10. Sputum and gastric washing cultures and

blood cultures, all repeated in timely fashion, are fundamental to accurate diagnosis. Finally, never overlook the possibility of *tuberculosis!*

### Acknowledgment

Case 1, Friedlander's bacillus pneumonia, is shown through the courtesy of Dr. John R. Durrance, Chief, Tuberculosis Section, Veterans Administration Hospital, Denver, Colorado.

### References

1. Brock, R. C.: Lung abscess. Charles C Thomas, publisher, Springfield, Illinois, 1952.
2. Christie, Amos, Middleton, J. G., Peterson, J. C., and McVickar, D. L.: Treatment of disseminated histoplasmosis with ethyl vanillate. *Pediatrics*, 7:7-18, (Jan.) 1951.
3. Craddock, W. L.: Pulmonary traits of systemic mycoses. *Mississippi Valley M. J.*, 75:28-37, (Jan.) 1953.
4. Forbus, W. D., and Bestebeutje, A. M.: Coccidioidomycosis; a study of ninety-five cases of the disseminated type with special reference to the pathogenesis of the disease. *Mil. Surg.*, 99:653-719, 1946.
5. Furcolow, M. L., and Grayston, J. T.: Occurrence of histoplasmosis in epidemics. *Am. Rev. Tuberc.*, 68:307-320, (Sept.) 1953.
6. Higginson, J. F., and Grismer, J. T.: Obstructing intrabronchial Hodgkin's disease; case report. *J. Thoracic Surg.*, 20:961-967, (Dec.) 1950.
7. Israel, H. L., et al.: Chronic disseminated histoplasmosis; an investigation of its relationship to sarcoidosis. *Am. J. Med.*, 12:252-260, (Feb.) 1952.
8. Jaffe, S. A.: Extrapulmonary Klebsiella pneumoniae infections; analysis of literature; report of two unusual cases with recovery. *J.A.M.A.*, 122:292-296, (May 29) 1943.
9. Jillson, O. F.: Mycology Medical Progress. *New England J. Med.*, 249:523, (Oct. 1) 1953.
10. Kirby, W. M. M., and McNaught, J. B.: Actinomycosis due to *nocardia asteroides*; report of two cases. *Arch. Int. Med.*, 75:578-591, (Nov.) 1946.
11. McVay, L. V., and Sprunt, D. H.: A long-term evaluation of aureomycin in the treatment of actinomycosis. *Ann. Int. Med.*, 38:955-966, (May) 1953.
12. Puckett, T. F.: Hyphae of coccidioides immitis in tissues of the human host. (In press).
13. Roque, F. T.; Ludwick, R. W., and Bell, J. C.: Pulmonary paragonimiasis; a review with case reports from Korea and the Philippines. *Ann. Int. Med.*, 38:1206-1221, (June) 1953.
14. Salzman, E.; Reid, J. H., and Ogura, G. I.: Cavernous metastatic pulmonary carcinoma; a report of two cases. *Dis. of Chest*, 23:678-685, (June) 1953.
- 14a. Schulz, D. M.: Histoplasmosis of the central nervous system. *J.A.M.A.*, 151:549-551 (Feb. 14) 1953.
15. Smith, C. E.: (a) Diagnosis of pulmonary coccidioidal infections. *California Med.*, 75:385-391, (Dec.) 1951. (b) Pathogenesis of coccidioidomycosis with special reference to pulmonary cavitation. *Ann. Int. Med.*, 29:623 (Oct.) 1948.
16. Smith, D. T.: The diagnosis and therapy of mycotic infections. *Bull. New York Acad. Med.*, 29:778, (Oct.) 1953.
17. Strang, C., and Simpson, J. A.: Carcinomatous abscess of the lung. *Thorax*, 8:11-28, (March) 1953.
18. Wallhauser, Andrew: Hodgkin's disease. *Arch. Path.*, 16:522-562, (Oct.) 672-712, (Nov.) 1933.
19. Winn, W. A.: Pulmonary mycoses—coccidioidomycosis and pulmonary cavitation; study of 92 cases. *Arch. Int. Med.*, 87:541-550, (April) 1951.

## THE EFFECT OF PENICILLIN UPON THE VIRULENCE OF C. DIPHTHERIAE

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THE PRESENT study was undertaken to investigate the inhibiting effect of penicillin upon the virulence of *Corynebacterium diphtheriae*. The need for such an investigation arose from the widespread use of antibiotic therapy in upper respiratory infections. In many instances, cultures taken from patients with suspected clinical diphtheria and under antibiotic therapy failed to show *C. diphtheriae*. The purpose of the study was to record the effect of antibiotics not only on the growth but also on the virulence of *C. diphtheriae*. Penicillin was chosen as the antibiotic for study since it is the one most commonly used.

The management of the patient with acute diphtheria and of the convalescent carrier is the joint responsibility of the clinician and the public health worker. The diagnosis of the disease and the treatment of the patient are prerogatives of the physician. The bacteriologist in the public health laboratory must furnish the physician with corroborating evidence by means of cultures from cases of acute and convalescent diphtheria. The bacteriologist should be informed whenever cultures are taken during penicillin therapy. If they are taken during that period, the physician should be cautioned that this is the period of greatest bacteriostasis and that cultures taken then may give rise to false or unreliable negative results.

Negative cultures at this period may mean that diphtheria goes undetected and that persistent carriers of *C. diphtheriae* may be released into the general population. The Minnesota Department of Health has recognized this danger and in recent years has added the query "Antibiotics used? When?" to the data cards accompanying diphtheria culture outfits. If the answer to the first question is affirmative, the following warning is typed on the report sent to the attending physician: "We note that this patient is receiving (antibiotics, penicillin, aureomycin, et cetera). We would advise that further nose and throat cultures be submitted at least forty-eight hours after such treatment is completed or terminated."

From the Minnesota State Board of Health, Division of Medical Laboratories.

### General Background

That penicillin has no influence upon the toxic effects of *C. diphtheriae* in the patient has been well established. Some investigators believe that penicillin therapy prevents complications from pyogenic organisms. All workers agree that the bacteriostatic effect of penicillin has a pronounced influence in reducing the persistence of *C. diphtheriae* in the upper part of the respiratory tract. The following is a brief review of more recent investigations on this subject.

Skinner,<sup>4</sup> in 1945, working with twenty patients, found that penicillin had a definite bacteriostatic effect upon *C. diphtheriae*. With adequate dosage he was able to eliminate *C. diphtheriae* in twelve of the patients in the first course of treatment.

Karellitz and associates,<sup>3</sup> in 1947, treated eighty diphtheria patients with antitoxin and intramuscular injections of penicillin. He found that 27.5 per cent remained positive at five days, in contrast to 100 per cent positive in controls receiving antitoxin only; 7.5 per cent remained positive at ten days, controls being 92 per cent positive; at fifteen days fewer than 5 per cent remained positive, controls being 85.7 per cent positive. Ten of fourteen convalescent carriers treated with intramuscular injections of penicillin cleared up by the twelfth day of treatment. These workers found some recurrence of positive cultures one to five days after penicillin therapy was stopped. They were convinced that some persistent carriers could be missed unless cultures were taken after cessation of therapy.

Weinstein,<sup>5</sup> in 1947, treated twelve patients with clinical diphtheria with antitoxin only. He found that *C. diphtheriae* disappeared in an average of 33.25 days. Twenty-six patients treated with antitoxin and penicillin failed to show *C. diphtheriae* in an average of 3.96 days.

Bruyon and Brainerd,<sup>1</sup> in 1950, found that sixty-two patients with clinical diphtheria treated with antitoxin only had the first consistent negative culture in 24.5 days on an average. In contrast, eighty-five patients receiving antitoxin and

## PENICILLIN AND *C. DIPHTHERIAE*—GIBLIN AND BAUER

penicillin became consistently negative in 17.7 days on an average.

### Recent Minnesota Experience

In 1952, only forty-five cases of clinical diphtheria were reported in residents of Minnesota; two cases in nonresidents were diagnosed in the state. There were only five deaths. This is a gratifying record, but its maintenance depends upon continued vigilance and cooperation of clinicians, laboratory workers and epidemiologists. An analysis of morbidity figures shows that sixteen of these forty-seven cases of diphtheria were reported from the age group one through nineteen years of age, whereas thirty-one cases occurred in patients twenty years or more of age. All the deaths occurred in the age group forty to sixty-five. It is significant that most of the cases and all the deaths occurred in the population that had a minimum of protection by immunization. Checking the records of release cultures completed at the beginning of the present work, we found complete culture reports in twenty-one; the results of virulence tests were positive in all twenty-one. Of these, seven were released from quarantine in a period of four to nine days and ten were released in a period of ten to twenty days; four were released in a period of twenty-one to thirty-one days. One patient received a second negative report in four days, two in five days, one in six days and two in seven days. The longest period of quarantine was thirty-one days. The average length of time before release was 13.05 days.

Data in regard to penicillin therapy were provided in only four of these instances. The studies of Hartley and Martin<sup>2</sup> on 457 diphtheria patients treated only with antitoxin indicate that 85 per cent were positive at five days and forty-two per cent remained positive at twenty days. These figures and the previously quoted data suggest the possibility that penicillin therapy was operative in securing negative release cultures in an average of 13.05 days in the Minnesota series. Not included in the group of twenty-one are two cases of clinical diphtheria in which the organisms failed to appear in cultures.

If it is assumed that penicillin is the cause of failure of *C. diphtheriae* to appear in cultures of clinical diphtheria and that its bacteriostatic effect has materially reduced the length of persistence of the organism in convalescence, then two serious problems arise: (1) Does the use of penicillin

as a bacteriostatic agent result in undetected clinical diphtheria? (2) Will the release of convalescent patients at an early date furnish a backlog of virulent carriers that may burst into epidemic proportions at a future date? On the other hand, does the bacteriostatic effect of penicillin on *C. diphtheriae* render the organisms nonvirulent?

### Present Study

In an attempt to throw some light on these problems, the present study on the inhibiting effects of penicillin on *C. diphtheriae* was undertaken.

**Procedures:** For the purpose of the study, six virulent strains of *C. diphtheriae* isolated in the current year were selected. Strains 1, 2 and 3 were obtained from patients who had clinical diphtheria with positive virulent tests reported respectively three, two and one-half and two months previously. Strain 4 was isolated from a person who has been a carrier for the past six years and whose last positive virulence test had been reported two months previously. Strain 5 was isolated from a newly detected carrier whose positive virulence test was reported one and one-half months previously. Strain 6 was isolated from a patient who had clinical diphtheria and whose positive virulence test was reported one and one-half months previously.

Serum agar was selected as the medium in which to incorporate varying amounts of penicillin. To check the suitability of the medium before the penicillin was added, the six strains of organisms were inoculated upon the serum agar. Abundance of growth and normal microscopic appearance of the organisms were noted. Virulence tests were done on the twenty-four-hour cultures. A test guinea pig was inoculated intracutaneously with 0.1 cc of a suspension of the cultures. A control guinea pig that previously had received 250 units of antitoxin was inoculated with identical material. All cultures showed strongly positive virulence. The control animal showed no reactions.

After these tests were completed, penicillin was incorporated in the serum agar in amounts of 5, 10, 100, 1,000 and 2,500 units per milliliter respectively. The six strains were inoculated upon the media, and growth was observed at the end of a forty-eight-hour incubation.

**Results.** Moderate to fair growth was noted in the tubes containing 5 units of penicillin. Micro-

## PENICILLIN AND *C. DIPHTHERIAE*—GIBLIN AND BAUER

**EFFECT OF FIVE UNITS OF PENICILLIN ON GROWTH  
AND VIRULENCE OF VIRULENT *C. DIPHTHERIAE*  
IN EIGHT SERIAL TRANSFERS**

Transfer	Cultures Viable in 5 u. Penicillin	Cultures Viable on Transfer to Löffler's	Cultures Nonviable on Both Media	Positive Virulence Test
1-2-3	6	—	0	6
4	3	2	1	5
5	2	3	0	5
6	2	2	1	4
7	2	2	0	4
8	2	0	2	2

scopic examination showed definite distortion of the organisms. No growth was discernible in the tubes that contained 10 to 2,500 units of penicillin. These cultures that failed to show growth in the presence of 10 to 2,500 units of penicillin were then transferred to penicillin-free Löffler's medium. Abundant growth was established in forty-eight hours. These transfer cultures on Löffler's medium were inoculated into guinea pigs, and positive virulence tests were obtained.

The serum agar cultures with penicillin concentrations of 10 to 2,500 units and with no apparent growth were placed in a refrigerator for a week. Then transfers again were made on penicillin-free Löffler's medium. Good growth was obtained after a forty-eight-hour incubation. Guinea pigs inoculated from the subcultures from tubes containing 10 to 2,500 units of penicillin showed positive results.

To show the effect of partial inhibition of growth of virulent *C. diphtheriae*, further studies were made on the six cultures that showed moderate to fair growth in the tubes containing 5 units of penicillin. These cultures were transferred to media containing 5 units of penicillin in a series of eight transfers over a period of two weeks. The accompanying table summarizes the results of such transfer upon the growth and virulence of the organism.

The third transfer showed a decided decrease in growth and an increase in the morphologic distortion of the organisms. This phenomenon increased with repeated transfers. On the fourth transfer, two of the cultures failed to grow on the penicillin medium but were established by transfer to Löffler's medium. One of the cultures failed to establish on both media. On the eighth transfer, only two cultures remained viable on the penicillin medium.

Even though the growth on penicillin medium

was scant and rough, positive virulence tests were obtained. In instances in which no apparent growth was obtained on penicillin medium but in which growth could be re-established by transfer to Löffler's medium, positive virulence persisted.

### Summary and Conclusions

The bacteriostatic effect of penicillin in amounts of 10 to 2,500 units on six strains of virulent *Corynebacterium diphtheriae* was demonstrated by the failure to produce visible growth after forty-eight hours of incubation. Transfers from these apparently nonviable cultures to Löffler's medium produced abundant growth with typical morphology. These cultures showed no loss of virulence as tested by inoculation of guinea pigs. Storage of the inhibited cultures in a refrigerator for a week did not result in loss of viability on transfer to Löffler's medium. Virulence of the organisms was not affected.

Cultures carried on medium containing 5 units of penicillin showed some inhibition of growth and some distortion of organisms at the initial stages. Progress over eight generations showed more scanty growth and more pronounced distortion. At the eighth transfer only two cultures remained viable. As long as cultures remained viable on the medium with 5 units of penicillin or from transfers therefrom, the virulence test remained positive.

### Conclusions

The following conclusions were reached as a result of this study:

1. The virulence of *C. diphtheriae* is not lost by partial or apparently complete bacteriostasis induced by penicillin.
2. Organisms that are partially inhibited or apparently completely inhibited on penicillin medium may be revived on Löffler's medium.
3. It is reasonable to assume that patients whose cultures are negative during antibiotic therapy may harbor virulent *C. diphtheriae* after therapy is terminated. Therefore it is recommended that:
  - (a) Cultures submitted from acute upper respiratory infections should be taken before antibiotic therapy to enable the laboratory to furnish reliable culture reports to the physician.

*(Continued on Page 598)*

# Seminar

## EISENMENGER'S COMPLEX

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Victor Eisenmenger, in 1897, reported the case of a cyanotic adult who at autopsy was observed to have a large ventricular septal defect. Twenty-five years later, Maude Abbott brought into focus the fact that in Eisenmenger's case the aorta was overriding the defect of the septum. She separated this malformation from the simple ventricular septal defect on one hand and the tetralogy of Fallot on the other and named it "the Eisenmenger complex." In the last few years, this syndrome has attracted much attention, as the diagnosis of the Eisenmenger complex is considered to be a contraindication for the performance of surgical procedures devised for the relief of cyanosis. Abbott recorded the basic anomalies to consist of high interventricular septal defect, dextroposition of the aortic valve overriding the septal defect associated with clinical manifestations of cyanosis, dyspnea, enlargement of the heart, diastolic murmurs, clubbing of the fingers and polycythemia. The embryological basis was documented by Abbott. The circulatory dynamics and physiology was discussed by Bing and associates.<sup>2</sup> Courmand and co-workers did cardiac catheterization studies in cases of Eisenmenger's complex.

### Definition

The Eisenmenger complex is usually presented as a cyanotic form of congenital heart disease consisting of a high defect of the ventricular septum, the aorta overriding the defect and dilatation of the pulmonary vessels, with an unobstructed pulmonary orifice. As in the tetralogy of Fallot, the hypertrophy of the right ventricle may be added as the fourth feature and the term tetralogy of Eisenmenger has been used by several authors.

The most important feature distinguishing the Eisenmenger complex from a simple ventricular defect is the presence of anoxemia in the former and its absence in the latter syndrome.

### Clinical Features

Altogether, thirty-eight cases with clinical and postmortem pathological findings have been reported in the literature. According to Selzer and

Prepared for Medical Grand Rounds at Ancker Hospital, Saint Paul, Minnesota, and edited by Dr. William F. Mazzitello.

Laguer,<sup>13</sup> these cases could be divided in three morphological groups: those fitting the classic concept of the syndrome (Group A); those in which the aorta was completely dextroposed (Group B); and those complicated by aortic valvular deformities (Group C). The second group, that of cases of ventricular septal defect with aorta arising from the right ventricle is included as representative of the Eisenmenger's complex and its inclusion will be justified in the following discussion.

Three patients survived over the age of fifty, and the majority died in the third or fourth decade of life. There were eighteen males and fifteen females. In five of the reported cases, sex was not mentioned (all of these five were between a few weeks of age to fourteen months). Twenty-six cases fall under Group A, eight cases under Group B and four cases under Group C.

Cyanosis was a constant feature, as it was present in Groups A and B in all patients with the exception of one infant and one adolescent. In the majority of cases of Group A, cyanosis was described as "moderate" in intensity. In most instances in Group B, it was severe. In sixteen cases of Group A the age at the onset of cyanosis was reported. It was present from birth or infancy in six cases; it developed in childhood in five and in adolescence or adult life in five. In Group B, cyanosis was present from birth or infancy in all cases. Group C was thought to be non-cyanotic. Cyanosis was specifically stated to be absent in three cases, and in the fourth one it was reported as present in association with severe cardiac failure. Polycythemia was reported in nine cases.

Clubbing was reported in twelve cases. A few signs and symptoms, such as chest deformity in five cases, underdevelopment in six cases, weakness and fatigue as a major symptom in four cases, epistaxis in three cases and hoarseness in one case due to pressure on the recurrent laryngeal nerve by the enlarged heart, have been reported in the literature.

Auscultatory findings were reported in twenty-six cases. In two cases, no murmurs were found; in two cases, a diastolic murmur only was noted. In all other cases, systolic murmurs were present but were variable in intensity, quality, location and conduction. The loud systolic murmur at the fourth left costal cartilage characteristic of the

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isolated ventricular septal defect was infrequently encountered. In Groups A and B, there was a frequent association of the systolic murmur with a diastolic blowing murmur best heard at the left sternal border. In Group C, of course, loud diastolic murmurs characteristic of aortic insufficiency were present. As a rule, in the cases of the Eisenmenger complex, there was a loud second sound present in the pulmonic area.

Electrocardiographic reports indicate that right axis deviation, the pattern of right ventricular hypertrophy or a right bundle branch block was, as a rule, present. Exceptions were rare and usually accountable for by complications.

The roentgenographic appearance of the cardiac shadow showed a remarkable uniformity. Of the twenty instances in which roentgenograms were described or reproduced, enlargement of the pulmonary artery was observed in nineteen. The one exception was in the case of a child in whom severe aortic insufficiency was present, which may have been a clinically more significant lesion than the Eisenmenger complex. The pulmonary artery shadow and that of its branches were usually described as prominently enlarged, often extreme in degree. Pronounced hilar pulsations were usually noted on fluoroscopy, and the pulmonary fields showed varying degrees of congestion, often severe. The heart was almost always enlarged:

Cause of death was given as follows:

Heart failure .....	15	Cerebral abscess .....	1
Endocarditis .....	5	Ruptured pulmonary artery aneurysm .....	1
Pneumonia .....	3	Cerebral thrombosis .....	1
Thoracotomy .....	3	Asphyxia .....	1
Anoxia .....	1	Unknown .....	6
Leukemia .....	1		

A review of the pertinent features of the cases with necropsy reveals that the clinical picture of this syndrome is well defined. It was shown that the late development of cyanosis has been overemphasized. In all cases with complete dextroposition of the aorta cyanosis is present from birth or infancy and is severe; in those with partial dextroposition of the aorta it frequently developed in infancy or childhood, not unlike the cyanosis of tetralogy of Fallot. The degree of cyanosis on the whole, however, is less severe than in the tetralogy of Fallot, and there are higher degrees of polycythemia. Prominent clubbing of digits is less frequently encountered in the Eisenmenger complex. Cyanosis is usually not present in cases associated with aortic insufficiency, and for that reason it is suggested that this combination be classified as the simple ventricular septal defect with aortic regurgitation.

Pulmonary hypertension appears to be a constant and important feature of the Eisenmenger complex. This may be demonstrated by direct pressure measurements or suggested by the striking dilatation of the shadow of the pulmonary artery and its branches in the roentgenogram, usually as-

sociated with intense pulmonary congestion and large amplitude of pulmonary vascular pulsations. This is also supported by the constant finding of the pattern of right ventricular hypertrophy in the electrocardiogram.

Murmurs in the Eisenmenger complex seem to be less characteristic than in uncomplicated ventricular septal defect. Systolic murmurs, often loud and harsh, are usually present and vary in location. Early diastolic murmurs at the left border of the sternum are common and are probably due to relative pulmonary insufficiency. Very loud diastolic murmurs, almost continuous, and changes in systemic pulse pressure have been reported in cases associated with aortic valve deformity. As a rule, the second sound in the pulmonary area is prominently accentuated.

The prognosis of the Eisenmenger complex appears to be fair and is comparable to that of other congenital defects of the less serious type. The average patient survives to early or middle adult life. Heart failure and bacterial endocarditis are important causes of death.

The following determinations will allow a complete and accurate laboratory diagnosis:

1. Hypertrophy of right ventricle by x-ray and pulmonary hypertension by cardiac catheterization may be determined accurately.

2. Information relative to overriding of the aorta may be secured by several methods; the cardiac catheter may be passed from the right ventricle directly into the aorta; the arm to tongue circulation time may be abnormally short; diodrast may be seen to pass directly from the right ventricle into the aorta, and finally, as will be shown, by analysis of oxygen and pressure relationships.

3. A high ventricular septal defect may be demonstrated by the presence of increased oxygenation in the upper portion of the right ventricle or pulmonary artery or by passage of the catheter through the defect. Thus it will be seen that each of the abnormalities comprising the Eisenmenger complex is subject to reasonably accurate determinations by one or more of the special methods outlined.

With cardiac catheterization, overriding of the aorta may be demonstrated in three ways: (1) passage of catheter from the right ventricle directly into the aorta, (2) simultaneous pressure records and (3) by demonstrating admixture of left and right heart blood in the aorta.

### Pathology

Pathological features of the Eisenmenger complex at autopsy were as follows: cardiac hypertrophy, almost uniformly affecting the right ventricle, a large basal ventricular septal defect, varying degree of dextroposition of the aorta and dilatation of the pulmonary arterial trunk to aneurysmal proportions.

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The defect of the ventricular septum was always located in the typical area, involving the membranous septum, its anterior part or the muscular septum just anterior to it. Its shape was usually oval, occasionally crescentic or round. The size of the defect varied from 1 to 3 cm. in the longest diameter in the fully developed heart. Since the size of the defect is of crucial importance from the standpoint of pathogenesis of the malformation and its hemodynamic effect, it was thought of importance to compare the size of the defect with that of the defects unassociated with other malformations (Roger's disease) and those associated with dextroposition of the aorta and pulmonary stenosis (tetralogy of Fallot). It is seen that the majority of uncomplicated defects of the ventricular septum are small; in the Eisenmenger complex moderate-sized defects occur. With the exception of the rare isolated defects in the lower septum, the location and shape of the defects in the three syndromes are identical. It should be emphasized that the largest defect in the ventricular septum encountered in any case of these syndromes occupies only a small portion of the septum, probably less than 10 per cent of its surface, in the fully developed heart. There is no gradual transition between larger defects of the ventricular septum and the complete absence of the septum.

The position of the aorta in relation to the septal defect has been usually reported as "overriding." In some cases, the degree of dextroposition of the aorta was estimated, and it is seen that all degrees of transition may be found, from cases in which the aorta originates almost entirely from the left ventricle to those in which it is completely dextroposed, i.e., originates from the right ventricle.

The other two features of the Eisenmenger complex, dilatation of the pulmonary artery and hypertrophy of the right ventricle, were consistently present throughout the series. Five cases showed serious vascular changes in the pulmonary arterioles.

Other pathological findings on autopsy include conditions like patent ductus arteriosus (three cases), patent auricular septal defect (three cases), hypoplasia of aorta (three cases), aneurysm of cusp of aortic valve (two cases), atypical coronary artery distribution (two cases), coarctation of aorta (two cases), anomalous distribution of vessels from arch (one case), retraction and insufficiency of aortic cusps (one case) and finally congenital tricuspid fetal endocarditis (one case), have been recorded.

### Morphological Relationship to Uncomplicated Defect of Ventricular Septum

It has been shown that the secondary features of the Eisenmenger's complex, the dilatation of the pulmonary artery and the hypertrophy of the

right ventricle are consistently observed in large, simple defects of the ventricular septum. The morphological distinction between the latter and the Eisenmenger complex, based on the presence or absence of dextroposition of the aorta, may present more difficulty at the autopsy table than is generally appreciated. It is of interest to note that Eisenmenger reported his original case as one of a ventricular septal defect and in a later article clarified his position concerning the overriding of the aorta. He presented evidence that the aorta is normally located in such a relation to the ventricular septum that if the membranous portion of the latter is defective it comes in contact with both ventricles. Thus, he believed that overriding of the aorta is a normal by-product of a large ventricular septal defect and not a developmental dextroposition. The unity of the two syndromes has been accepted in the German literature.

In order to account for the morphological similarity between larger ventricular septal defects with or without the dextroposition of the aorta, and in consideration of the generally accepted fact that the aorta may be embryologically malposed in such cases, a different way of unifying the two syndromes has been suggested. It was thought that the same process of maldevelopment which brings about transposition of the arterial trunks in its severest forms, and is responsible for partial dextroposition of the aorta (overriding) with or without pulmonary stenosis, in less severe forms, causes the isolated high ventricular septal defect in its mildest form. This view finds further support from studies done:

1. It was shown that within the Eisenmenger complex all degrees of dextroposition of the aorta can be found.
  2. The otherwise identical defects are, on the average, larger in the Eisenmenger complex (or tetralogy of Fallot) than in the uncomplicated form.
  3. A striking example is presented in a case of Selzer,<sup>13</sup> in which the fetus had a defect of the ventricular septum appearing identical with that of the mother, except for the dextroposition of the aorta, which was present in the mother but not in the fetus. Yet it was the fetus that had an abnormal origin of the coronary ostia, which is considered characteristic for the transposition malformation.
- Although Eisenmenger's original interpretation appears in part incorrect, his observation helps to emphasize the difficulty which is often encountered at autopsy in deciding whether or not dextroposition of the aorta was present during life. It is highly probable that the physiological overriding of the aorta can be accentuated by changes in pressure relationship, in topography of the arterial trunks related to gradual dilatation of

## EISENMENGER'S COMPLEX—PRASAD

the pulmonary artery and in other factors. Thus, overriding of the aorta need not be considered a fixed morphological feature.

### Pulmonary Vascular Changes and Their Relation to Cyanosis

The uniform finding of pulmonary hypertension in cases of Eisenmenger's complex studied by cardiac catheterization suggests that these changes are an essential part of the syndrome; it was shown also that pulmonary arteriolar resistance is extremely high.

The reported changes in the pulmonary arterioles belong pathologically to the same group as those found frequently in other conditions associated with pulmonary arterial hypertension [mitral stenosis, cor pulmonale and those associated with large pulmonary arterial flow (septal defects, patent ductus arteriosus)]. The changes in the intima and media show some similarity to systemic arteriolar changes in systemic hypertension. In severe cases of pulmonary arteriolar disease, the changes resemble those of malignant hypertension.

From the physiological standpoint it is clear that the pulmonary arteriolar changes represent evidence of long-standing severe pulmonary hypertension. It has been suggested, however, by Burwell, Taussig and Blalock that pulmonary vascular disease interferes with oxygen exchange in the lungs and thus it is responsible for cyanosis. This opinion was based on consideration that oxygen inhalation raised the arterial oxygen content and that in the Eisenmenger complex the circulation to the lungs is not "inadequate." Yet, neither of these factors helps in determining the mechanism of cyanosis. There is no valid reason to separate the Eisenmenger complex from all other forms of congenital heart disease with cyanosis in which it is evident that anoxemia is caused by an admixture of venous blood in the systemic circulation. On the contrary, one can present evidence that in Eisenmenger complex, caval blood enters the aorta; this is shown by hemodynamic studies and by angiography. Moreover, a causal relationship between pulmonary hypertension and arteriolar disease on one hand and cyanosis and anoxemia on the other has not been definitely established. Finally, Bing and his associates interpreted the finding of a close check between blood flow determination in Eisenmenger complex performed by the oxygen and carbon dioxide methods as evidence of a normal pulmonary oxygen exchange. One can further cite the case of Soulard and his collaborators as illustrating the lack of relationship between cyanosis and the pulmonary factors. In spite of proved severe pulmonary hypertension and arteriolar disease, the arterial oxygen saturation was normal, as apparently the co-existing aortic insufficiency "cor-

rected" the overriding of the aorta to a point that caval blood could not enter it.

It seems reasonable to believe that anoxemia and cyanosis in the Eisenmenger complex are due to a "shunt" mechanism and the pulmonary venous blood is fully oxygenated, such as is shown directly in the tetralogy of Fallot and the anoxic form of atrial septal defect.

### Circulatory Dynamics<sup>3</sup>

A discussion of the hemodynamics of Eisenmenger's complex can best be opened by summarizing facts about which there appears to be reasonable certainty.

1. *Pathological Facts.*—(a) The defect of the ventricular septum is always located in the basal, subaortic portion of the septum and occupies only a minute portion of the septum, with most of it intact. (b) The aorta may originate mostly from the left ventricle, may arise mostly from the right ventricle, or may occupy an intermediate position. All degrees of transition can be found between the two extreme positions. (c) The pulmonary vascular changes indicative of high arteriolar resistance can usually be demonstrated.

2. *Clinical Facts.*—(a) Systolic pressure in the right ventricle and the pulmonary artery are equal and are always elevated in the Eisenmenger's complex but are occasionally normal in simple ventricular septal defect. This is shown by a collection of results of cardiac catheterization. (b) In many cases, perhaps the majority, the pressure elevation in the right ventricle-pulmonary artery system is such that systolic pressure readings are identical with the pressure readings in the aorta and the left ventricle. (c) Increased oxygenation of pulmonary arterial blood and decreased oxygenation of systemic arterial blood prove that there is a cross shunt, or pre-mixing of caval and pulmonary venous blood. The systemic flow may equal the pulmonary flow or one may exceed the other, without any consistency in this relationship.

3. *Experimental Facts.*—Studies on experimental defects of the ventricular septum show that a fistulous connection between the two ventricles of a dog's heart comparable to a medium-sized human ventricular septal defect results in flow of blood through the fistula from the higher pressured left ventricle to the lowered pressured right ventricle. No equalization of pressure in the two chambers takes place, but a slight fall in the left and a rise in the right ventricular systolic pressure occur.

It would seem from the foregoing summary that the most characteristic feature of Eisenmenger's complex is the presence of severe pulmonary hypertension, which is invariably demon-

## EISENMENGER'S COMPLEX—PRASAD

strated in this syndrome, in contrast to the atrial septal defect, the ventricular septal defect and the patent ductus arteriosus where it is only occasionally present. The consistency in the observation of severe pulmonary hypertension and the frequency with which equal pressures in the two arterial trunks are demonstrated indicate that increased pulmonary resistance plays an important role in the dynamics of the circulation of the Eisenmenger complex.

It has recently become apparent that in certain anomalies of the heart, pulmonary hypertension may have to be present from birth as a condition for the survival of the patient. The reason for this is the fact that the physiological postnatal adjustment, during which an equal pressure in the pulmonary artery and the aorta changes into a high resistance and high pressure systemic circulation and a low resistance and low pressure pulmonary circulation, could prove fatal in those cases in which both trunks originate from a common source. The malformation in such a case creates a pressure pump which has two outlets; the quantity of blood entering each of them is in inverse proportion to the resistance offered. Thus, a low resistance pulmonary outlet could draw all the blood, with none available for the high resistance systemic circulation. In such cases, survival depends on equal resistance in the pulmonary and systemic circuits, which can be achieved by (a) systemic hypotension or pulmonary hypertension or by (b) a mechanical obstruction of the low resistance outlet, as pulmonary stenosis. The obvious conditions to which this concept of a "double outlet ventricle" applies are partial transposition of the arterial trunks, in which both great vessels originate from the right ventricle and the trilocular heart, in which both trunks arise from a common ventricle. A somewhat similar situation exists in some cases of patent ductus arteriosus with coarctation of the aorta in which the right ventricle maintains the pulmonary circulation and the lower part of the systemic circulation.

It is obvious that in the variant of the Eisenmenger complex with complete dextroposition of the aorta (Group B), one is dealing with a "double outlet ventricle" in which pulmonary arteriolar constriction and/or disease has to be present from birth for survival, since no protective pulmonary stenosis is present. However, in the classic Eisenmenger complex where the aorta is merely overriding the septal defect, one has to search for another factor explaining the pulmonary hypertension.

It was shown that an experimental ventricular septal defect produces a pathway for a left to right shunt. One can assume, however, that as the defect in the ventricular septum becomes larger and approaches the size of the aortic orifice the left ventricle becomes a "double outlet ventricle," in which case the low resistance right

ventricle can draw all the blood away from the systemic circulation, unless the resistance in the right side of the heart is raised either by pulmonary stenosis or by pulmonary arteriolar constriction and hypertension. Pressure relationships between the two ventricles in cases of Eisenmenger complex and Fallot's tetralogy suggest that in the majority of them the defect is in effect large enough to name the left ventricle a "double outlet ventricle."

The concept of the "double outlet ventricle" as applied to the Eisenmenger complex, the trilocular heart and other similar syndromes is based on fundamental principles of hemodynamics and has to be postulated to explain the fact that survival in the post-embryonic life is at all possible with some of these malformations. However, the mechanism of the production of the protective pulmonary hypertension in such cases, the stimulus for the development of pulmonary arteriolar constriction and/or disease from infancy, is as yet unknown.

Another problem requiring analysis is that of the physiological significance of the "overriding" aorta. It is commonly assumed that an "overriding" aorta collects blood from both ventricles. Such a statement ignores the fact that normally the systolic pressure in the right ventricle is lower than the diastolic pressure in the aorta, and, if normal relationships were preserved, blood could not ordinarily flow from the right ventricle to the aorta. Deoxygenated caval blood can enter the aorta (a) if the systemic circulation is maintained by the right ventricle in complete dextroposition of the aorta; (b) if pressures in the two ventricles are equal, in which case the overriding position of the aorta facilitates turbulence and mixing of blood in the deficit; (c) if the pressure in the right ventricle is slightly lower than in the left, in which case turbulence may still throw right ventricle blood into the aorta, perhaps aided by the Venturi phenomenon.

The importance of the topographic relationship of the aorta to the ventricular septal defect in the production of anoxemia is exemplified by observations of Soulie and his associates in their cases of the Eisenmenger's complex associated with aortic valvular deformity. In one such case, the aorta was seen at autopsy to be dextroposed over the septal defect so that morphologically this was an instance of Eisenmenger's complex, but the longitudinal axis of the aorta was observed to be rotated counter clockwise, probably as a result of changes brought on by aortic valve deformity and insufficiency. This shift corrected the overriding position of the aorta, and the patient was found to have a normal oxygen saturation, even though severe pulmonary hypertension was present. Significantly, two other patients with the Eisenmenger's complex associated with aortic insuffi-

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# Laboratory Aids to Medical Practice

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## THE SURGEON AND THE MYCOLOGIST

LYLE A. WEED, M.D.  
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THE USE of surgical procedures for treatment in certain selected cases of mycotic infection is well established. However, the surgeon must keep constantly in mind that certain fungous infections may be encountered unexpectedly during operations for therapeutic or diagnostic purposes. The selective therapeutic effect of certain drugs useful for treating such infections makes it necessary to know precisely the nature of the fungus.

### Fungal Infections

The pathogenic fungi frequently important to the surgeon are *Blastomyces*, *Histoplasma*, *Coccidioides*, *Cryptococcus*, *Sporotrichum*, *Nocardia*, *Actinomyces* and *Aspergillus*. Recent work would indicate that *Actinomyces* may be classed more properly as a bacterium than as a fungus. However, for the sake of convenience, it will be considered as a fungus in this presentation. With the exception of *Blastomyces* and *Coccidioides*, infections due to fungi are world-wide in distribution. Except for *Sporotrichum*, fungi are likely to produce lesions in the lungs. These may be solitary lesions simulating bronchogenic carcinoma or they may be multiple, bilateral and widespread, simulating extensive tuberculosis. Many of them may excavate, producing cavities that enhance the clinical similarity to tuberculosis. Like other intrapulmonary lesions that become chronic, they may metastasize to vital areas, such as the brain, kidneys or spinal column. It is important, therefore, that the nature of the infection be established as early as possible because many of these metastatic lesions may be prevented by modern chemotherapeutic agents. Since tuberculosis is the most common cause of chronic infection in the lung and since most of the mycotic infections

simulate tuberculosis, the intrapulmonary lesions frequently progress to fatal termination while extensive bacteriologic studies of sputum, gastric washings and bronchial secretions over months or even years continue to be reported "negative for tubercle bacilli."

### Diagnosis

It is important, therefore, when studies are made relating to intrapulmonary lesions, that cultures for fungi should be made as routinely as are cultures for tubercle bacilli or smears for malignant cells. The added expense is small and is insignificant when contrasted with the benefits to the patient. It is indeed pitiful to see patients treated with first one and then another antibiotic, empirically, intermittently or inadequately, while the condition progresses and metastasizes to the brain because careful mycologic studies have not been made. Such studies may determine that the patient needs iodides, sulfonamides or stilbamidine, or that the dosage of penicillin should be increased severalfold. The surgeon who sees such patients in consultation frequently can be of great help by requesting that proper search be made for fungi.

In most cases the diagnosis of fungous infections must be made by isolation of the organism. Skin tests have been tried and in some instances have been useful. Most patients who have coccidioidomycosis are likely to give a positive cutaneous reaction after intradermal injection of coccidioidin, but in the experience at the Mayo Clinic most of those who have chronic localized forms of this disease give negative reactions, even when *Coccidioides immitis* is isolated from the lesion. In the remainder of the mycotic infections already mentioned, skin tests are unreliable in diagnosis; in some cases, they even may be misleading.

Dr. Weed is from the Section of Bacteriology of the Mayo Clinic.

## THE SURGEON AND THE MYCOLOGIST—WEED

### Histopathology

Many times when a surgeon removes tissue for biopsy complete reliance for a diagnosis is placed on the histopathologic interpretation. Regardless of the site of the lesion, such a procedure may be entirely inadequate. The human body can react to stimuli in a limited number of ways and the response to infection with a fungus may closely simulate that seen in other infections. Many times the organisms are not visible in the histologic sections or, if found, may not be sufficiently characteristic for accurate identification. It is frequently impossible to determine on a morphologic basis whether a given organism is *Blastomyces dermatitidis*, *Blastomyces brasiliensis*, *Coccidioides immitis* or *Cryptococcus neoformans* but it is extremely important to know the true identity. *Sporotrichum*, *Nocardia* and *Actinomyces* are rarely, if ever, visible in sections stained with the usual hematoxylin and eosin. The masses of material frequently called "sulfur granules," when stained and subjected to culture, may be found to contain not *Actinomyces* but streptococci, micrococci, *Nocardia*, *Cephalosporium*, *Aspergillus* or no organism at all. It is extremely important to the patient to know the nature of these "granules." The surgeon should see that the proper specimen in adequate amount

is sent for bacteriologic and mycologic studies. The patient's limb or life may depend on it.

Therefore, the surgeon should consider the possibility of a fungous infection in any condition simulating tuberculosis or neoplasm. He should attempt to establish the diagnosis as early as possible. This is best done by isolation of the organism, either from sputum, bronchial washings or material taken directly from the lesion.

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This is the eighteenth in a series of editorial reports sponsored by the Minnesota Society of Clinical Pathologists and designed to foster closer relationships between the practicing physician and the pathologist.

Together with the preceding one, entitled "The Surgeon and the Bacteriologist," this report emphasizes the growing importance of bacteriologists and mycologists in the modern practice of medicine. The essential role played by such specialists in the field of clinical pathology has been spotlighted by the advent of new drugs and antibiotics.

Emphasis must be placed on the point that the histopathologic picture is not always specific in either bacterial or mycotic infections and that the appearance of tissue cannot be substituted diagnostically for isolation of the causative organism. Surgical pathologists were somewhat reluctant at first to accept this stand, but increasing experience has proved its correctness.

Reprints of most of this series of reports are available from the authors or the chairman of the editorial committee of the Minnesota Society of Clinical Pathologists.

GEORGE G. STILWELL, M.D.  
Chairman, Editorial Committee,  
Mayo Clinic.

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### POLIO VACCINE TRIAL NEEDS PHYSICIANS' AID AS IT MOVES INTO EVALUATION PHASE

More than 600,000 children have completed three inoculations, in the field test of the trial polio vaccine developed by Dr. Jonas E. Salk of the University of Pittsburgh. The emphasis now shifts to the evaluation study under the direction of Dr. Thomas Francis, Jr., University of Michigan School of Public Health. The validity of the evaluation is dependent upon data gathered on poliomyelitis cases in the test groups, *including those children in the first three grades who did not get vaccine.*

In addition, data on cases among family members of participating children are an integral part of the study. Since the number of poliomyelitis cases among the test groups may not be large, it is essential that all cases are completely reported. Early diagnosis, prompt re-

porting and follow-up, and the securing of necessary epidemiological information and laboratory specimens are important factors in the evaluation.

An outline of procedures and copies of necessary forms have been sent to local and state health authorities. It is important that physicians in areas where vaccinations were not given, co-operate in the study by notifying local or state health officers of cases occurring among children who participated in the trials and then migrated to another area and children who go to summer camps. Local health officials also need information on participating children who receive injections of Gamma Globulin.

This phase of the study will depend, to a large degree, on the whole-hearted co-operation of practicing physicians.

# President's Letter

## SUMMER SLUMP?

Most of us along about this time of year find ourselves a little on the lazy side. We are inclined to let the oppressive heat of summer capture our senses to some extent, and a consequent summer slump is likely to occur.

But there are many things in medical organization which should not be allowed to leave our consciousness entirely. Simply because late spring meetings are over, and a recess is in effect until fall, we should be aware that our attention is needed in many projects of vital importance.

One of these is the American Medical Education Foundation. Most of us have heard many pleas for contributions to this fund. One of the most recent was that presented to the House of Delegates at our June meeting in Duluth. The worthwhile nature of this project was emphasized there, and facts and figures were presented which pointed up the literal urgency of this program.

Since the fund was begun in 1951, 298 Minnesota physicians have given a total of \$26,279.00 into this fund. In return, the University of Minnesota medical school has received \$66,956.00—an excellent return for our investment.

The American Medical Education Foundation was founded and has been sponsored by the American Medical Association, which has given \$500,000.00 annually to the fund, so that all money raised could be meted out to the nation's seventy-nine medical schools, without encumbrance.

One of the main reasons for the initiation of such a group was the threat of Federal subsidy. Because of the need for funds by medical schools throughout the country, Congress considered a bill which would provide these funds at government expense. Thus, the group was formed, and it was felt that if about ten million dollars could be raised over a period of years, the need would be eased sufficiently so that there would be no need for Federal subsidy.

Minnesota doctors have not given their full share toward this important fund, as the above figures indicate. The need is still great. It should be pointed out that all funds contributed can be earmarked by the giver for whatever medical school he wishes.

It is hoped that the traditional summer slump will not jeopardize this important work in Minnesota. This offers an excellent opportunity for Minnesota doctors to do their share in insuring the maintenance of high medical school standards in the United States. It is a national problem, for the seventy-nine medical schools in fifty-six cities are charged with the responsibility of turning out an estimated 6,000 physicians annually.

It is clearly our job to see that schools can maintain and improve these standards—a challenge which continues, regardless of the traditional summer slump.



President, Minnesota State Medical Association

# Editorial

ARTHUR H. WELLS, M.D., *Editor*; HENRY G. MOEHRING, M.D., and JOHN F. BRIGGS, M.D.

## STATEWIDE CANCER DETECTION

A RECENT EDITORIAL in MINNESOTA MEDICINE has emphasized the cost of finding early cancers in the Cancer Detection Center at the University of Minnesota. The same editorial also encouraged limitation of x-ray examinations of internal organs to persons presenting symptoms of visceral disease; this would be in contrast to the Cancer Detection Center program of studying symptom-free people for internal cancers by means of appropriate x-ray techniques when certain established criteria are present. The directors of the Cancer Detection Center wish to reply to this editorial and define the relationships of the Detection Research Center to a generalized community-wide cancer detection effort.

It is evident from past experience that for purposes of over-all service to the people of a state a single cancer detection center cannot hope to fulfill the needs of the population. However, statewide examination service is not the basis of existence of the Minnesota detection center. Rather, it functions dually as a testing unit to pioneer in improvements of practical diagnostic methods, and as a source of stimulation for both lay and professional groups. The reticence of already heavily overburdened physicians to take on the routine examination of apparently well persons in the manner now necessary for adequate cancer screening is readily understandable. Without a central effort of this kind, however, sponsored by the State Council of the Minnesota Medical Association and supported generously by the Minnesota Division of the American Cancer Society, any service program of early detection of cancer would drift about like a rudderless ship.

Undue emphasis upon cost factors is hard to defend in the light of present mortality statistics for most serious cancers. If we consider the over-all yearly expenditures in the Cancer Detection Center, compared with the number of examinations performed, it is apparent that the average cost of an examination has been slightly under \$25.00. The cost per cancer found has been slightly over \$3,000.00. If we add precan-

cerous lesions to the cancers found, the cost for detection of either a precancerous lesion or a cancer is \$180.00. Is it reasonable to believe that patients found to be free of cancer in the Detection Center receive nothing for the token fee which they contribute and the small expenditure of research funds allotted to their examination? I think not.

If one sets out to evaluate life in terms of dollars and cents, it would appear that the tremendous expenditure of money yearly in the United States for the treatment and care of poliomyelitis patients is a rather wasteful expenditure. By and large, severely affected polio cases are likely to be liabilities to the community after the cure of the disease, rather than an asset. Is such a thought to be the motivating factor in forsaking the cure and rehabilitation of poliomyelitis patients? Similarly, can anyone place a monetary valuation upon a group of lives, either prolonged for a few years or saved through early cancer detection?

Even though the numbers of cancers in any given organ found in our Cancer Detection Center during six years of operation is not great, an appraisal of the figures immediately reveals a significant increase of patients surviving cancer therapy when their disease was detected in the absence of symptoms. Such a simple comparison of results argues strongly for the benefits to be derived from earlier diagnosis. A review of current publications reporting five-year survivals for serious cancers, such as gastric cancer, impresses one with the significance of our present survivals in the asymptomatic patients found in the Detection Center. When we consider the great discrepancy between survivals of patients with cancer of the rectum and colon when the lesion is limited to the mucosa and submucosa as against lesions where cancer has spread to regional lymph nodes (eighty to ninety per cent in the first group and thirty to thirty-five per cent in the second group), the value of early diagnosis is again apparent.

If every doctor's office program were aimed at a thorough cancer examination only of pa-

## EDITORIAL

tients with symptoms, results probably would not be much better than we currently see reported from medical and surgical centers around the United States. It is only with an increased stimulation and emphasis upon the *yearly examination of well people* that the every doctor's office program can be expected to achieve its maximum benefit with an increased percentage of long-term survivors.

With an increasing enlightenment of the lay public through the efforts of state and county chapters of the American Cancer Society, coupled with an earnest desire on the part of most physicians in the State of Minnesota to perform a searching and complete examination for cancer at the patient's request, we may well see a continuing improvement in the number of five-year survivals from serious malignancies. Coincident with this general effort, there should be a continuing search at the Cancer Detection Center for better, and more specific methods of diagnosis.

When a new specific and general cancer test appears, it can best be tried under the controlled conditions of a research center; in such ways your Cancer Detection Center has contributed and will continue to contribute to the general effort. The Director of the Cancer Detection Center urges doctors throughout the State to take an active part in the *examination of well people for early, asymptomatic cancers*.

Claude R. Hitchcock, M.D.  
Director, Cancer Detection Center  
University of Minnesota

### A REACTION TO CRITICISM

DURING the last year, several articles appeared in the lay press concerning unethical surgical procedures, such as fee-splitting and ghost surgery. The impetus for these articles has become credited, rightly or wrongly, to the American College of Surgeons and its director, Dr. Paul Hawley. At the annual meeting in Chicago in October, 1953, college officials called in reporters and, to quote the *New York Times*, "Served notice on the rest of the medical profession that it was ready to meet all comers in its year-old campaign to eradicate surgical practices which the college considered unethical."

The reaction of most physicians to this announcement has been complete agreement with

the objectives and complete disagreement with the methods. Following publication of an article in *Collier's* AMA Secretary George Lull sent the editor a telegram of sharp protest, as did the American Academy of General Practice; in contrast, the Director of the American College of Surgeons sent a message of commendation.

This sensational, dogmatically critical, quixotic approach to a problem of such seriousness is unfortunate. It is unworthy of the American College of Surgeons, an organization which has done more than any other to improve hospital care and raise surgical standards, yet which is now becoming an anathema to organized medicine. In doing so, the American College of Surgeons dissipated its great potential for accomplishing a fine and worthy task, one which in some sectors is urgently in need of doing.

This problem is rightly one for the Joint Commission on Accreditation and the American Medical Association; their efforts to be implemented by the American College of Surgeons, the American College of Physicians, the American Academy of General Practice, and others. These, with effective and sound methods to achieve a fully and correctly informed public, can accomplish the desired result. It is similar to the situation regarding Christian ethics—they will work miracles if we would but try them!

We all live together in this House of Medicine. Where this House is dirty, let's flush it out! If parts of it are rotten, then tear them down and build anew! But sensational, iconoclastic and misinterpreted articles in the lay press hurt us all. We can only hope that important and influential men *within the home* will see this in time, and do enough.

Chas. C. Cooper, M.D.

EDITOR'S NOTE.—If the drastic action of the American College of Surgeons and Dr. Paul R. Hawley of calling upon public opinion to halt certain unethical practices fails to produce anything more than righteous indignation in the ranks of organized medicine in Minnesota, we shall have lost a most opportune time for action, and the exposé will then have been a miserable failure.

The responsibility for a planned and co-ordinated action in this field properly belongs in our County and State Medical Societies. Any organization so far removed from the individual physician as the Joint Commission on Accreditation will do no better than the American College of Surgeons.

"Our profession creates its eminence through deeds, not words, and through meeting human needs, not in satisfying our own" (from John P. Bowler, M.D.).

## EDITORIAL

### PYHICIAN, HEAL THYSELF

LET US not allow self-interested, self-appointed groups unjustifiably to air our rare and minor defects in the public press. Let us seek remedies for our supposed ills through our own County and State Medical Societies, the American Medical Association, and the American Academy of General Practice; in accordance with rational medical ethics.

In 1903, the American Medical Association declared that the split of a fee without knowledge of the patient was an unethical practice. The American Academy of General Practice in Cleveland, in March, 1954, re-affirmed its unequivocal opposition to fee-splitting, ghost surgery, and other unethical medical practices, as it had done in previous meetings. It decried public statements and other publicity detrimental to medicine, recently aired by some apparently self-appointed spokesmen for the profession.

Certain basic intraprofessional rules should be generally accepted by physicians. No special selfish group should have a surgical or hospital monopoly. Every doctor in good standing should be able to hospitalize his patients. No group should inspire self-laudatory public statements for themselves or statements which imply incompetence of other groups. It must be recognized that general practitioner surgeons do most of the ordinary surgery in this country with excellent results, as shown by morbidity and mortality studies and patient satisfaction. Self-study, assisting competent surgeons, doing surgery under supervision, and observing surgery have produced surgeons equal in ability to those with more formal training, and should be recognized as methods of training.

The general practitioner who acts as family physician, as a rule, does only what he is qualified to do. He is the backbone of the practice of medicine. He can care adequately for most of his patients' illnesses, and he is more interested than anyone else in securing specialist assistance, when necessary, to promote his patients' welfare. Every patient should be under the direct and immediate supervision of his personal physician, with that physician making referrals when necessary.

The American Academy of General Practice requires that each member complete 150 hours of postgraduate training each three years, in order to retain his membership in the organization. All

physicians should be required to keep up with the new developments in medicine. Physicians should follow the teachings of Christianity and Hippocrates, and be willing to teach other physicians their knowledge and techniques.

The referring general practitioner and the consultant or surgeon should each be adequately remunerated in proportion to the services rendered. The family general practitioner should have a place in the operating room as surgeon, assistant or observer, according to his abilities and desires, and the patient should be aware of the duties of each doctor in his complete care. This will induce harmony and satisfaction for the patient and his doctors, prevent the existing evils, improve the intraprofessional relations of physicians, and increase patient satisfaction.

The American Academy of General Practice, at the inspiration of Dr. Merrill Shaw, a member of its Board of Directors, who recently died of cancer, is fostering a new project, "*A Family Doctor for Every Doctor's Family*," which proposes that every doctor secure a family physician for himself and his immediate family in the hope that physicians' early mortality can be decreased and their families' health protected.

A "*Family Doctor for Every Family*" would reduce the cost of medical care and greatly promote better intraprofessional and public relationships and understanding of physicians.

There should be more equitable representation of all branches of medicine on the Joint Commission on Accreditation of Hospitals, with its control vested in the House of Delegates of the American Medical Association. A democratically selected, joint commission could clear up the rare abuses. The hospital staffs have an important responsibility in encouraging physicians to promote voluntary high standards of medical care.

Postgraduate medical education should be available to any physician so that he may improve his ability in any line of work at any time he wishes. No group should deny this opportunity to the general practitioner. Most general practitioners have a major interest in some branch of medicine and a minor interest in others. In justice to themselves and their patients, there should be unlimited opportunities for them to improve their abilities.

Grievance Committees in county and state medical societies should be publicized and become

## EDITORIAL

more active in improving intraprofessional and public relations.

We physicians, through democratic processes, must work out improved methods of conducting our professional affairs and improving our personal health and the health of the public for the benefit of all.

J. A. COSGRIFF, M.D.  
President, Minnesota  
Academy of General Practice

## SEMINAR SECTION

Manuscripts of the miniature monograph type are being accepted for publication in the Seminar section. Practically complete presentations of limited medical subjects of wide interest are being solicited. "The Eisenmenger Complex" by Ananda Prasad in this issue is the first of a series. Your contribution will be appreciated.

## CHEMOTHERAPY FOR TUBERCULOSIS

### The Problem

Many patients now being discharged from sanatoria may continue to receive anti-tuberculosis chemotherapy; some may receive chemotherapy before entering the sanatorium and a few get this treatment without ever going to the sanatorium. These practices raise problems affecting the state and local health departments, the public health nurses, practicing physicians, and the patients themselves. The following recommendations are made to assist in the management of these patients.

### Recommendations

Any patient who is to receive chemotherapy for tuberculosis should have a careful evaluation of his condition to insure the proper utilization of all available methods of therapy. Chemotherapy is only one important part of the total treatment of a patient with active tuberculosis. This is particularly important when, for some special reason, sanatorium care is not definitely planned for the patient. Under these circumstances the physician in charge is obviously responsible for prescribing the drugs, including the specific form of the drug, the exact dosage, the route and frequency of administration and the duration of chemotherapy. The person responsible for giving the treatment, such as a nurse, should be given this information in writing.

When a patient is to receive anti-tuberculosis chemotherapy after dismissal from the sanatorium, his private physician or the physician at the sanatorium, should be notified simultaneously, and in advance if possible, so that they may plan for the care of the patient at home.

A statement prepared by the Committee on Tuberculosis, Minnesota State Medical Association, May 17, 1954.

They should be given complete information about the drugs being used, including the specific form of the drug, the exact dosage, and the route and frequency of administration and total duration of treatment with drugs.

Although a nurse may be given responsibility for the administration of the drugs the patient must remain under the supervision of a physician, either his private physician or the physician at the sanatorium and should be examined by him at least once every two months. The patient or nurse in charge should report to the physician any untoward reaction to the drugs but the physician should make the decision to continue or stop treatment with the drug suspected of causing the reaction. This is particularly important as interruptions in the course of the treatment seem to increase the chance that drug-resistant strains of tubercle bacilli will occur.

The drugs used most frequently today are streptomycin, isoniazid (INH) and para-aminosalicylic acid (PAS).

Streptomycin may be given as streptomycin, dihydrostreptomycin, or streptoduoicin, which is a mixture of equal quantities of streptomycin and dihydrostreptomycin. These drugs are available as the sulfate or the calcium chloride complex and may be bought already in solution or as a powder to be dissolved in sterile distilled water. They must be given intramuscularly, the usual dose for adults varying from one gram daily to one gram twice a week. The most common toxic reactions are dermatitis, drug fever, dizziness, and deafness. Many patients receiving some form of streptomycin complain of transitory numbness and tingling particularly about the mouth.

Isoniazid is usually given orally, parenteral preparations being reserved for critically ill patients who cannot swallow the tablets. The usual dose for adults varies from 150 to 300 mgm. per day, divided into two to three doses. The most common toxic reactions are peripheral neuritis, irritability, and drug fever.

PAS is usually given orally as the sodium or calcium salt, in tablets, granules, capsules, or powders. The usual daily dose is twelve grams of PAS divided into three or four doses. The equivalent daily dose of the sodium salt is sixteen grams. Preparations for parenteral administration are available. Irritation of the gastrointestinal tract producing anorexia, nausea, vomiting, and diarrhea may occur when the drug is given orally in the recommended dose. This can be diminished by giving PAS along with food. Other reactions are dermatitis and drug fever.

### Reporting

All reports to the Minnesota Department of Health of cases of tuberculosis should include information as to anti-tuberculosis chemotherapy already received by the patient.

# The Dean's Page

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## SHORT COURSES IN TECHNOLOGY

A recent high school graduate was referred by her family physician to the secretary of the county medical society for information about training in medical technology. The secretary of the society told her about the splendid four-year course in medical technology at the University. She replied that she could not afford such a long course and asked about the one-year courses offered by the commercial schools. He advised against these schools but failed to mention to her the one-year program for laboratory aids inaugurated a year ago by the University. The result was that this young woman went to a business college.

I mention this because there is an urgent need for more trained young women in laboratories, in x-ray departments, and in doctors' offices. In fact, the course for laboratory aids was established at the request of the Minnesota State Medical Association and with the co-operation of the Minnesota Society of Medical Technologists, the Minnesota Society of Clinical Pathologists, and the Minnesota State Board of Health.

This course is one year in length, with six months spent in basic instruction at the University and six months in laboratory work under supervision in a hospital laboratory in the Twin Cities. The course does not prepare young women to be medical technologists, but it does prepare them to perform simple laboratory procedures under supervision in hospitals or in doctors' offices.

Somewhat similar to this is the new three-month course offered by the University in the basic sciences pertinent to x-ray technology. To be admitted to this course, an individual must be accepted for x-ray training in one of the approved courses in a Minnesota hospital.

Enrollment in these courses has been disappointingly small and must be increased to justify their continuation. The reason for the small enrollment probably is that the programs are new and not well known. We hope that this will be corrected by the physicians of the state, at whose request the courses were established.

HAROLD S. DIEHL, M.D.  
*Dean of Medical Sciences  
University of Minnesota*

# Medical Economics

Edited by the Committee on Medical Economics  
of the  
Minnesota State Medical Association  
George Earl, M.D., Chairman

## ILO CONVENTION GETS "THUMBS DOWN"

According to a recent *AMA Washington Letter*, President Eisenhower has forwarded to Congress the International Labor Organization's convention on minimum standards of social security, with a recommendation that it not be ratified.

It will be recalled that the convention, which was adopted by the ILO in 1952, if adopted by individual nations, would become similar to a treaty, and in effect, would be the supreme law of the land. The convention covers nine fields: Medical care, sickness benefits, unemployment benefits, old age benefits, employment injury benefits, family benefits, maternity benefits, invalidity benefits and survivor benefits. A government is considered to have ratified the convention if it promises to meet the requirements in three of the nine fields.

The *Washington Letter* states: "The medical care section stipulates that a country may qualify as ratifying if it agrees to provide one of the following: (a) a system of compulsory health insurance, (b) private, voluntary health insurance 'administered by public authorities under established regulations' set by law, or (c) private, voluntary health insurance administered by insurance companies but under government 'supervision.' Half the population would have to be covered."

Quoting the President's words in transmitting the convention to Congress, the letter states:

"is . . . regarded as not suitable for ratification but rather for referral to the appropriate federal and state authorities for their consideration."

Accompanying the transmittal was a summary of comment from all affected federal departments and agencies, which pointed out that federal laws already are in accord with two of the points, old

age insurance and survivors insurance. On the other points, the agencies came to the same conclusion as the President, namely that these issues are within the jurisdiction of state governments and "that therefore the convention is not appropriate for ratification" by Congress.

Because there is no time limit for ratification of the convention (treaty), this matter presents a constant possibility of thrusting compulsory health insurance, or some form of government-controlled health insurance on this country. Presumably, the convention has been studied from 1952 until the present time by various agencies and departments of the federal government.

## Reconsideration Apparent

Apparently the delayed study of the implications in the treaty have caused the President and his advisors to reconsider the original U. S. delegation's favorable vote. The U. S. delegation voted in favor of the convention originally, but a spokesman for the delegation was quoted as saying at that time that this did not imply that the U. S. would accept the entire convention. Ratification would require a two-thirds vote of the Senate. Also, the State Department pointed out, in 1952, that the U. S. delegation agreed that the convention should not be recommended to the Senate for ratification as a treaty (which would be binding on this government and all the states), but should instead be passed along to Congress and the states for final disposition.

The U. S. delegation consisted of Senator Murray (D., Mont.) and Assistant Secretary of Labor, Philip M. Kaiser, representing government; George P. Delaney of the AF of L, representing employes, and Charles P. McCormack, president of McCormack Tea & Spice Co., Baltimore, employer representative.

The recent summary also noted that while signatories to the convention agreed to bring it be-

## MEDICAL ECONOMICS

fore their respective legislative bodies, "it is entirely within the discretion of the competent authority of each country to determine whether any legislation is to be enacted." The federal agencies concurring in this opinion were Commerce, Interior, Justice, Labor, Navy and Health, Education and Welfare Departments, and the Civil Service Commission.

Although the outcome of the convention bears close watching, it can be hoped that the treaty, which caused so much concern among medical and other groups, will die a natural death because of the President's recommendation.

### "GIVE-AWAY" SHOW GETS MEDICAL CHECK-UP

A new tack in medical public relations has revealed that medicine has become somewhat concerned over the impressions of medicine given by certain radio and television shows. Questioning the heartbreak stories of participants on "Strike It Rich," it is thought that the viewing audience, running into millions, has been left with the impression that financial assistance was needed in paying for the high cost of medical care.

In checking on these matters, representatives of the AMA and the Medical Society of the County of New York contacted the producer of the show, in an effort to reach some understanding. The interview was successful, apparently, for it was reported that "we were most impressed with the sincerity of . . . (the producer) in his desire to assist the medical profession in any way possible. He apparently has great admiration for the medical profession and in no way wished to discredit the profession on his show."

Subsequently, the producer asked the AMA to investigate two cases. In one case, in which the total medical bill had accumulated to \$6,000, it was found that the family was covered by Blue Cross and had used this service. Also, it was found that at no time was the patient without medical care because of financial difficulties.

### Case Dismissed

In both of these cases, according to a recent *AMA Secretary's Letter*, the investigations revealed that the individual had been "adequately taken care of at the community and state level, and, consequently, there was little basis for the appeal. This information was made available to

(the producer) and both cases were considered ineligible to participate on his program."

This type of "preventive medicine" has again proved valuable to the profession as a whole. In averting an unpleasant situation before it occurs, the profession's lay representatives on a national level have demonstrated that an ounce of prevention against poor public relations is well worth more than a pound of cure.

### JOINT COMMISSION ISSUES ACCREDITATION FIGURES

The May issue of the *Bulletin of the Joint Commission on Accreditation of Hospitals* carries a summary of accreditation figures as of December 31, 1953. The figures show that of the total number of registered hospitals, all types and sizes, 43.6 per cent are accredited. The bulletin points out however, that "if the hospitals of less than twenty-five beds are eliminated (and these hospitals are not now eligible for accreditation), more than half, or 51.8 per cent, are accredited."

The bulletin further points out that the figures show that the greatest emphasis must be placed on the area of the smaller hospital in order to improve the total picture in regard to accreditation of hospitals. A committee is now studying methods to assist the smaller hospitals in earning accreditation.

### Basic Standards Developed

A set of standards for the Commission's guidance have been developed over the years of experience of the original accrediting agency, the American College of Surgeons and the work of the Joint Commission. This publication, "*The Standards for Hospital Accreditation*," is the basic operating document for the commission. It is regarded as a sound and wisely-developed measuring stick for the evaluation of hospitals. The Board of Commissioners has stated that it would act slowly in making any changes in the basic standards, but that methods for review are being established to take changing conditions into consideration.

### POPULATION SHOWS LARGE INCREASE

The population of the United States continues to show an annual increase over and above previ-

ous years. In 1953, the population increased 2,700,000, bringing the total at about 161,200,000. These figures are from a *Statistical Bulletin* of the Metropolitan Life Insurance company. The bulletin states: "This large increment, exceeding somewhat the previous high gain registered in 1952, reflected not only a record-breaking number of births, but also a low death rate and a moderate increase from immigration." Breaking down this statement further, the bulletin says:

"The new high record for births was not far short of the four million mark. The actual number, including an allowance for unregistered births, was more than 3,950,000, or nearly twenty-five per 1,000 population. The births in 1953 were nearly 2 per cent greater than in the preceding year and more than 50 per cent higher than in 1940. The year just ended was the seventh in succession in which births exceeded three and one-half millions. In the past decade, the number of babies born reached the remarkable total of more than 35 million."

#### Infants Deaths Low

Also, according to the bulletin, infant mortality declined in 1953, establishing a new low estimated at twenty-eight per 1,000 live births, or slightly below the previous minimum recorded the year before. This decline in infant mortality represented a decline of 30 per cent from that a decade ago and of more than 50 per cent from that two decades ago.

The general mortality rate was also at a low level. The 1953 death rate was 9.6 per 1,000, or about the same as in the preceding year, which established a new minimum. The bulletin states that "this record is especially impressive because 1953 was marked by an outbreak of respiratory disease early in the year and a severe hot spell in late summer, both of which brought a rise in mortality over the seasonal normal.

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... one of the purposes of a journal is to provide a means for the dissemination of the opinion of its readers ... It is not likely that all the letters received can be published, therefore somebody has to select those most suitable for this purpose and to reject others. ... Fortunately, there will be many who will not approve the editor's decision, for that keeps all concerned alert and on their toes, but he is fortified by the knowledge that a measure of disapproval is inescapable, and that all he can do is to endeavor to see that it moves round as much as possible, and does not stagnate in one place.—*Lancet*, April 3, 1954.

#### EISENMENGER'S COMPLEX

(Continued from Page 584)

ciency were non-cyanotic, which adds great weight to the observations and explanation of Soulard and his co-workers.

In the light of the previous discussion, one can define the Eisenmenger complex to consist of (a) a high localized defect of the ventricular septum, (b) a position of the aortic orifice in relation to the defect which permits an admixture of venous blood to enter the aorta, as evidenced by anoxemia and (c) an absence of significantly elevated resistance at the pulmonary outflow tract of the right ventricle. Secondary features of the syndrome, not included in the definition but constantly found in the entity are (a) strikingly elevated resistance at the pulmonary arterioles with organic changes within them; (b) severe pulmonary hypertension or even equalization of pressure in the two circulations; (c) hypertrophy of the right ventricle and (d) dilatation of the pulmonary artery and its branches.

#### Bibliography

1. Alexander, Fred and White, Paul D.: Ann. Int. Med., 1:64 (July) 1947.
2. Bing, R. J., Vandam, L. D., and Gray, F. D.: Bull. Johns Hopkins Hosp., 80:323 (June) 1947.
3. Bond, Vernon F. Jr.: Am. Heart J., 42:424, 1951.
4. Cosby, Richard S.; Levinson, David C.; Griffith, George C.; Zinn, Willard J., and Dimitroff, S. P.: Am. J. Med., 11:31, 1951.
5. Dillion, W. H., and Schreiber, Jr., H.: Am. J. Physiol., 159:281 (Aug.) 1948.
6. Glazebrook, A. J.: Brit. Heart J., 5:147, 1943.
7. Goldberg, H.; Silber, E. N.; Gordon, A., and Katz, L. N.: Circulation, 4:343, 1951.
8. Hawley, J. G.; Little, R. C., and Feil, H.: Circulation, 1:321 (March) 1950.
9. Hurst, W. W., and Schem, F. R.: Am. Heart J., 36:144 (July) 1948.
10. Jarcho, Saul: J. Mt. Sinai Hosp., 18:59 (May-June) 1951.
11. Plachta, Aaron and Speer, Francis, D.: J. Pediat., 42:325 (Mar.) 1953.
12. Saphir, O., and Lev, M.: Am. Heart J., 21:31, 1941.
13. Selzer, Arthur, and Laguer, G. L.: Arc. Int. Med., 87:218, 1951.
14. Taussig, H. B., and Semans, J. H.: Bull. Johns Hopkins Hosp., 66:156, 1940.

## AMERICAN MEDICAL ASSOCIATION

### House of Delegates—Résumé of Proceedings

San Francisco, June 21-25, 1954

Fee splitting, osteopathy, closed panel medical care plans, veterans' medical care and the training of foreign medical school graduates were among the major subjects of discussion and action during the sessions of the House of Delegates at the American Medical Association's 103rd Annual Meeting June 21-25 in San Francisco.

Named as president-elect for the coming year was Dr. Elmer Hess of Erie, Pennsylvania, who, until his election, was serving as a member of the House of Delegates and as Chairman of the Council on Medical Service. Dr. Hess will become president of the American Medical Association at the June, 1955, meeting in Atlantic City, succeeding Dr. Walter B. Martin of Norfolk, Va. Dr. Martin took office at the Tuesday evening inaugural session in San Francisco's Palace Hotel.

The House of Delegates voted the 1954 Distinguished Service Award of the American Medical Association to Dr. William Wayne Babcock of Philadelphia for his outstanding contributions to medicine and humanity. Dr. Babcock, who was professor of surgery and clinical surgery at Temple University School of Medicine from 1903 to 1944, received the award from Dr. Martin at the Tuesday evening inaugural ceremony.

The final registration total for the San Francisco meeting was expected to reach approximately 35,000, including more than 12,000 physicians.

#### Fee Splitting

The House adopted a supplementary report of the Reference Committee on Miscellaneous Business which recommended acceptance of a Judicial Council report on the subject of billing and made the additional recommendation "that the House of Delegates resolve that it firmly opposes fee splitting, rebating or payment of commissions in any guise whatsoever, and that it further opposes any mechanism that encourages this practice."

The Judicial Council report included the following statements:

"The Judicial Council is of the opinion that the only new facet concerning this subject that has come up recently is the case of joint billing to some of the non-profit insurance companies. In many cases these insurance companies insist on a joint or combined bill, but the bill is being paid in most instances by two checks. This is not considered unethical and all insurance plans which do not pay the individual physician in this manner should be urged to do so."

"The Judicial Council is still of the opinion that when two or more physicians actually and in person render service to one patient they should render separate bills.

"There are cases, however, where the patient may make a specific request to one of the physicians attend-

ing him that one bill be rendered for the entire services. Should this occur it is considered to be ethical if the physician from whom the bill is requested renders an itemized bill setting forth the services rendered by each physician and the fees charged. The amount of the fee charged should be paid directly to the individual physicians who rendered the services in question.

"Under no circumstances shall it be considered ethical for the physician to submit joint bills unless the patient specifically requests it and unless the services were actually rendered by the physicians as set out in the bill."

#### Osteopathy and Medicine

Four resolutions dealing with the osteopathic problem were considered. The House accepted a recommendation by the Reference Committee on Medical Education and Hospitals and adopted a Supplementary Report of the Board of Trustees on a Report of the Committee for the Study of Relations Between Osteopathy and Medicine:

"The justification or lack of justification of the 'cultist' appellation of modern osteopathic education could be settled with finality and to the satisfaction of most fair-minded individuals by direct on-campus observation and study of osteopathic schools. The Committee, therefore, proposed to the Conference Committee of the American Osteopathic Association that it obtain permission for the Committee for the Study of Relations between Osteopathy and Medicine to visit schools of osteopathy for this purpose.

"The Conference Committee favorably recommended this proposal to the board of trustees of the American Osteopathic Association which considered it at a special meeting on February 6-7, 1954. It has referred the question to its house of delegates which will act upon the proposal in July, 1954. If the action of the house of delegates of the American Osteopathic Association be favorable, the on-campus observations can be carried out in the fall of this year.

"The Committee therefore recommends:

"1. That no action be taken on the report at this time and that final action be deferred until December, 1954.

"2. That the Committee be continued until December, 1954, in order to be available to evaluate education in schools of osteopathy should the house of delegates of the American Osteopathic Association act favorably upon the recommendation of its Conference Committee."

#### Closed Panel Plans

The much-publicized New York resolution, calling for several changes in the Principles of Medical Ethics relative to participation in closed panel medical care plans, was considered by the Reference Committee on Miscellaneous Business. That committee made the following recommendation, which was adopted by the House:

"In the discussion before your reference committee on this resolution, it became apparent to the committee that clarification and interpretation of the Principles of Med-

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## PROCEEDINGS—AMERICAN MEDICAL ASSOCIATION

ical Ethics in relation to prepaid medical care plans are desirable. As set forth in the bylaws, the Judicial Council has jurisdiction on all questions of medical ethics.

"Therefore, your reference committee recommends that the House of Delegates request the Judicial Council to . . . investigate the relations of physicians to prepaid medical care plans and render such interpretations of the Principles of Medical Ethics as the Council deems necessary, and report to the House of Delegates not later than the next annual meeting of the Association.

"The committee further recommends that the New York resolution be referred to the Judicial Council for consideration in connection with this investigation."

The New York resolution, among other suggested changes, would add the following new paragraph to Chapter I, Sec. 4, "Advertising," of the Principles of Medical Ethics:

"It should be understood that any medical care plan, company, or organization which advertises for subscribers and directs such subscribers to a restricted panel of physicians for medical care is advertising for the benefit of the physicians involved."

### Veterans' Medical Care

Accepting a report by the Reference Committee on Legislation and Public Relations, the House adopted two strong resolutions condemning the present practice of establishing service-connection for veterans' disabilities by legislative fiat. In recommending passage of both resolutions, the committee said:

"The study of the chronological expansion by law and regulation, together with evidence presented of pending legislation now before a Congressional Committee, emphasize all too clearly the imperative need of decisive action on the part of the American Medical Association.

"It is the opinion of the Committee that the time is at hand when the American Medical Association and its component societies should go all out in preventing this unscientific method of determination of service-connected disabilities, and that we respectfully request that copies of these resolutions be transmitted to the Congress of the United States and other appropriate federal agencies."

In connection with veterans' medical care, the House also adopted recommendations by the Reference Committee on Insurance and Medical Service which reaffirmed the policy on non-service-connected disabilities, established at the 1953 annual meeting, and which commended the informational program carried out since then by the Committee on Federal Medical Services of the Council on Medical Service.

### Foreign Medical Graduates

Three resolutions and a Board of Trustees supplementary report were submitted to the House regarding the evaluation of foreign medical school graduates, a subject which attracted major interest earlier this year at the annual Congress on Medical Education and Licensure in Chicago. The Reference Committee on Medical

Education and Hospitals spent much of its time listening to the ideas and proposals of various state medical societies, state licensing boards, members of the Council on Medical Education and Hospitals and others. The reference committee recommended that "the intent and aims of this Supplementary Report and the three resolutions can best be met by referring the entire problem to the Council on Medical Education and Hospitals for further study. It is recommended that the Council report at the Interim Session in 1954 regarding the progress relative to this study." The House adopted the reference committee's recommendations.

### Seal of Acceptance

The Council on Medical Service presented a supplementary report outlining the difficulties encountered in conducting the Seal of Acceptance program, and recommending discontinuance of the Seal of Acceptance for voluntary health insurance plans. The report said that the standards and principles of the program will be maintained as guides and recommendations for all groups operating or establishing plans. The House, on recommendation of the Reference Committee on Insurance and Medical Service, adopted the Council report, thus terminating the Seal of Acceptance program for voluntary health insurance plans.

### Registration of Hospitals

The House also approved a Board of Trustees report calling for discontinuance of the registration of hospitals by the Council on Medical Education and Hospitals and suggesting that the Joint Commission on the Accreditation of Hospitals be requested to undertake the registration of hospitals in addition to its present accreditation activities.

### Miscellaneous

Among a wide variety of other actions, the House also:

Voted to continue the holding of the annual Clinical Meetings;

Approved the establishment of a program of medical military scholarships with appropriate safeguards limiting the number of students involved;

Approved the extension, on a voluntary basis, of the Medical Education for National Defense program which currently is in operation in five medical schools as a pilot study, and

Authorized the Council on Scientific Assembly to conduct a thorough study of the use of tape recordings of the material presented at meetings of the Council, and asked for a report at the December meeting.

## PROCEEDINGS—AMERICAN MEDICAL ASSOCIATION

### Opening Session

Highlights of the opening House session on Monday were selection of Dr. Babcock as recipient of the Distinguished Service Award and the addresses by Dr. Edward J. McCormick of Toledo, then president of the Association, and Dr. Martin, then president-elect.

Dr. McCormick called upon the medical profession to take the guesswork out of medical costs by adopting average fee schedules on an area or regional basis. The Reference Committee on Reports of Officers later suggested that the Board of Trustees make a study of such programs where they already are in operation, and the House approved.

Dr. Martin, in his opening session address, declared that the most urgent problem before the medical profession is that of financing hospital services to make them more generally accessible. In his presidential inaugural address, Dr. Martin said that physicians are duty-bound to keep themselves informed on public matters affecting the medical welfare of the people, and he also urged doctors to "reach back farther than the disease" in treating their patients.

### Special Citations

Two special citations were presented by the Association during the San Francisco meeting. During the presidential inauguration ceremony Dr. McCormick presented an award to a fellow Toledan, Dr. Nicholas P. Dallis, for his outstanding health educational service as the writing member of the team that produces the illustrated feature, "Rex Morgan, M.D." At the closing House session on Thursday, Dr. Martin presented a special citation to Smith, Kline & French Laboratories of Philadelphia for "pioneering use of television in bettering the health of the nation." The plaque was accepted for the company by Mr. Francis Boyer, president.

The closing session also brought the announcement that the California Medical Association had presented a check for \$100,000 to the American Medical Education Foundation.

### Election of Officers

The election at the closing session brought the following results, in addition to the selection of Dr. Hess as president-elect:

Dr. Clark Bailey of Harlan, Ky., was named vice president.

Dr. David B. Allman of Atlantic City and Dr. F. J. L. Blasingame of Wharton, Texas, were re-elected to their positions on the Board of Trustees.

Also re-elected were Dr. George F. Lull of Chicago, secretary; Dr. J. J. Moore of Chicago, treasurer; Dr. James R. Reuling of Bayside, N. Y., speaker of the House of Delegates, and Dr. Vincent Askey of Los Angeles, vice speaker.

Dr. J. Morrison Hutcheson of Richmond, Va., was named by Dr. Martin as a member of the Judicial Council to succeed Dr. Edward R. Cuniffe of New York, who served as Council chairman for many years. Dr. Homer Pearson of Miami, Fla., was elected new chairman.

Dr. W. Andrew Bunten of Cheyenne, Wyo., was elected a new member of the Council on Medical Education and Hospitals, succeeding Dr. W. L. Pressly of Due West, S. C. Dr. Charles T. Stone, Sr., of Galveston, Texas, was re-elected to the same Council. Both terms run to 1959.

Dr. Floyd S. Winslow of Rochester, N. Y., was re-elected to the Council on Constitution and By-Laws for a term ending in 1959.

Dr. Joseph D. McCarthy of Omaha Neb., was re-elected to the Council on Medical Service for another term running to 1959. To fill the vacancy created on the same Council by Dr. Hess' resignation following his election as president-elect, Dr. Robert L. Novy of Detroit, Mich., was selected.

The House of Delegates also chose New York City as the place for the 1957 annual meeting, San Francisco for 1958 and Atlantic City for 1959. Previously selected were Atlantic City for 1955 and Chicago for 1956. The dates of next year's meeting in Atlantic City are June 6-10.

J. ARNOLD BARGEN, M.D.  
O. J. CAMPBELL, M.D.  
GEORGE EARL, M.D.  
F. J. ELIAS, M.D.  
*(Delegates)*

### THE EFFECT OF PENICILLIN UPON THE VIRULENCE OF C. DIPHTHERIAE

*(Continued from Page 579)*

(b) Cultures taken for the purpose of releasing patients from restrictions should be taken no earlier than forty-eight hours after antibiotic treatment has been discontinued.

### References

1. Bruyon, H., Brainerd, H.: Penicillin in the Treatment of Diphtheria. *Am. J. Sc.*, 219:408, 1950.
2. Hartley, P., Martin, C. J.: Proc. Roy. Soc. Med. London, Sec. Epidemiol. and State Med., 13:277, 1919-1920.
3. Karelitz, S., Wasserman, L. R., Moloshok, R. E.: Penicillin in the treatment of diphtheria and diphtheria carriers. *J. Pediat.*, 30:1-18, 1947.
4. Skinner, J. W.: Penicillin in persistent diphtheria. *U.S. Naval M. Bull.*, 45:264-6, 1945.
5. Weinstein, L.: Treatment of acute diphtheria and the chronic carrier state with penicillin. *Am. J. M. Sc.*, 213:308-14, 1947.

# Public Health

## THE PHYSICIAN AND VITAL STATISTICS

In almost every medical article he reads, the physician may see and study statistical tables relating to the measurements of human life. He probably gives little thought to the fact that his own cases play a significant part in the construction of such tables. Perhaps he does not fully realize the value of statistics as guides in the many factors influencing man's well-being.

Actually each individual physician's records form an essential part of the vast collection maintained by the State Board of Health. From this storehouse of facts, nosology brings back to the physician reports of current trends in causes of death, together with comparisons and interpretations of such trends that may have direct application to cases under his care. Many indications of answers to problems faced by the physician in his day-to-day practice may be found in the statistical bases that underlie a particular case. From correct reports amassed from all sources and statistically treated, many a physician may obtain sound public health guidance in the treatment of his individual patients.

Vital statistics constitute the basis of all medical research. For instance, the "Medical and Health use" items on the uniform Certificate of Live Birth are of great value in analyzing infant and maternal deaths. Such items are considered confidential and are therefore not included in the certified copy of a birth certificate given to a person requesting it. This information, however, is indispensable for accurately determining trends in natality and mortality throughout the state.

### The Physician's Responsibility

Every practicing physician shares in the responsibility to help the statistician compile a body of accurate and complete vital data that may be of great value to other physicians. Lately there has appeared a tendency to abbreviate causes of death in the medical certification on Certificates of Death. This practice often causes confusion and delay. The state registrar of vital statistics has to communicate with the physician concerned in order to ascertain just what he meant by the

letters he used to record a particular cause of death. Querying follow-ups are annoying to the physician, and answering them may well involve far more time than would have been needed to fill in the certificate completely in the first place. Furthermore, if the death certificate must be produced in court in a civil or criminal proceeding, the physician may be called upon to explain items that are not clear. Every practitioner will want to avoid such encroachments on his time. He can at least minimize them by writing out causes of death accurately and completely, thus removing all doubt as to what, in his professional judgment, brought about each death.

In some cases the physician may require extra time to complete his medical certificate—for instance, when autopsy findings require study or consultation. In such a situation he should write the words "diagnosis deferred" after the heading of the "Medical Certification." He should at the same time date and sign this certificate and forward it to the vital statistics section of the State Board of Health. Upon receipt of such certificates—Incomplete but promptly filed—the state registrar will forward to the physician a special Medical Certification form on which he may record the cause or causes of the death after he has ascertained them to his satisfaction. The same procedure should be followed by coroners.

### Help from Board of Health

All vital statistics offices in the United States are now operating under rules of the World Health Organization. The Minnesota State Board of Health is increasing its efforts to obtain on all death certificates the cause-of-death certification provided for under these rules. Some physicians in the state still appear to lack full understanding of these accepted procedures. Because the State Board of Health desires to remedy this situation, it proposes to provide help through this page in subsequent issues. The material published for the guidance of physicians will present a number of illustrative cases in an attempt to clarify coding points that may be troublesome.

J. W. BOWER, M.P.H., Director  
Departmental Administration  
Minnesota Department of Health

# Minneapolis Surgical Society

Meeting of January 7, 1954  
President Robert Tenner, M.D., in the Chair

## TUMORS OF THE HAND

MICHAEL L. MASON, M.D., F.A.C.S.  
Chicago, Illinois

The hand is the site of a great variety of tumors. Some of these are among the most frequent tumors seen, e.g., ganglia, synovial cysts, epidermoid cysts. Others occur with great rarity on the hand, e.g., sarcoma, sebaceous cysts. Some seem to be almost peculiar to the hand, e.g., enchondromas, glomus tumors, ganglia, implantation cysts and isolated xanthomas of the tendon sheaths.

The diagnosis of tumors of the hand should be made early because of the ease of examination and as a corollary the cure rate should be high. The removal of benign appearing skin lesions will appreciably reduce the incidence of malignant tumors since in many instances it appears that benign lesions are the precursors of malignancy.

In scarcely any other part of the body does trauma and irritation seem to play such an important role in the development of malignancy. Sunlight and other types of irradiation, chemical and mechanical irritants, old scars, and puncture wounds have all been shown to be factors leading to the development of malignant tumors, particularly of carcinoma. This observation certainly points the way to prophylactic measures and likewise emphasizes the possible medicolegal aspects of skin cancer in industry.

All tumors of the hand are treated preferably by surgery. While it may be admitted that some will respond to irradiation therapy, this treatment often fails and is followed by the development of an irradiation damage to the skin often of more serious import and demanding more extensive surgery than excision of the original lesion. Biopsy of tumors of the hand should consist in their complete removal, and if the lesion is sufficiently serious, frozen section should be carried out while the patient is still on the table. In this way further surgery, if indicated, can be carried out then and there. Removal of the deep tumors of the hand demands a thorough knowledge of the anatomy of the hand. Many of the benign tumors simply displace nerves and tendons, grow around them or insinuate themselves between them. A digital nerve, for example, may be deeply buried in a groove of a benign xanthoma from which it must be carefully dissected free. The deep lipomas may follow tendon sheaths and require extensive dissection.

Some idea may be gained as to frequency of the various tumors of the hand from an analysis of some 700 tumors. Of these tumors, approximately one-third were ganglia. Another third was made up of four tumors in about equal numbers—xanthomas, epidermoid cysts, angiomas, and irradiation carcinoma. One-sixth was made up of carcinoma (not developing on the basis

of irradiation), lipoma, fibroma, neuroma, and enchondroma, again in approximately equal numbers. The remaining 1/6 comprised the remainder of the hand tumors: synovioma, glomus tumor, fibrosarcoma, giant cell tumors, osteosarcoma, osteoma, Ewing's tumor, osteoid osteoma, lymphangioma, sweat gland carcinoma, myxoma, leiomyoma, metastatic tumors, et cetera.

It is convenient to classify these tumors according to the tissue from which they take their origin—skin, fibrous tissue, fatty tissue, bones and joints, tendons, tendon sheaths and joint capsules, nerves, blood and lymphatic vessels, and muscles. There is not 100 per cent agreement as to whether some of the tumors are actually tumors in the strict sense of the word, e.g., xanthoma, ganglion, angioma, and glomus tumor. Certain of them, like the fibroma and fibrosarcoma, neurofibroma and neurosarcoma, are still confused as to actual status.

### Tumors of the Skin

The common wart while probably not a true tumor and usually treated by neglect, home remedies, or the dermatologist, comes to the surgeon's attention under one of several circumstances. The subungual wart is especially troublesome; it causes an ugly lesion under the nail, is resistant to ordinary therapy, and is awkward to deal with even surgically. It is a nuisance to the patient and becomes tender and inflamed quite easily. The surgeon also sees the wart which has failed to respond to treatment or which persists without change over many years and then begins to grow or to ulcerate. He also sees the common wart when it has failed to respond to usual treatment, has broken down and become infected, or has ulcerated after various types of home care. The surgeon likewise sees the wart when other more serious changes have occurred—when it develops spreading ulceration or a cauliflower-like proliferation, often following mechanical injury. The surgeon also sees the palmar wart which, because of its location, is frequently subject to trauma.

In all such instances noted above, it is my feeling that surgical treatment is indicated. Usually simple excision will suffice with suture closure, although a wide excision may be needed and occasionally a skin graft may be necessary to close the defect. In case of the subungual wart, the raw surface left beneath the nail must always be closed by a skin graft and a certain amount of nail deformity must be accepted as a sequel. If there is any question as to possible malignancy of the lesion, a frozen section may be indicated at operation. A subungual wart, which proves to be a carcinoma may re-

## TUMORS OF THE HAND—MASON

quire amputation of the digit. Also, what may at first instance appear to be a simple wart may prove to be a melanoma and likewise require amputation of a finger.

*Keratoses, hyperkeratoses and squamous papillomas* are not infrequently on the backs of the hands of individuals who have been out in the sun and weather a great deal, in elderly people, sailors, farmers, et cetera. Such lesions in themselves are of slight moment, but they should not be ignored since they may be the precursor of malignancy.

The *epidermoid or inclusion or implantation cyst* is a quite frequent tumor of the hand which resembles clinically the ordinary sebaceous cyst. It differs from the sebaceous cyst in that it is derived strictly from epithelium, is lined by squamous cell layers as is the skin, and is filled with desquamated epithelial cells and debris. It occurs very frequently on the hand, whereas the sebaceous cyst is very rare on the hand. There is quite a literature about these tumors. Some authors have contended that they develop as the result of the implantation of bits of skin beneath the surface as the result of puncture wounds, hence the name traumatic epithelial cyst or implantation cysts, or, since occasionally foreign material is found in them, they are also called inclusion cysts. On the other hand, it would seem that some of them are the result of proliferation of cellular rests of epithelium which on proliferation produces cystic cavities. They have been produced experimentally. In a few instances the skin over them has shown a small scar as evidence of earlier trauma. In an occasional one a foreign body, such as the tip of a thorn has been found.

The *implantation cyst* occurs especially frequently on the volar surface of the hand and digits. A favorite location is at the base of the palm over or between the regions of the metacarpophalangeal joints. They are sometimes seen in association with Dupuytren's contracture in which case they may be due to drawing down and eventual pinching off of a tiny islet of skin by the attachments of the fascia to the corium of the overlying skin. They occasionally become infected, particularly those lying at the base of the palm. Ordinarily, however, they produce few symptoms and are simply a cosmetic blemish or interfere with the use of the hand. They should be removed intact surgically and do not recur.

The *sebaceous cyst* is a distinct rarity on the hand, although it may occur on the dorsum. It is treated by excision, as anywhere else in the body.

### Carcinoma of the Hand

Carcinoma comprises about 90 per cent of all the malignant tumors of the hand. It likewise makes up close to 10 per cent of all hand tumors. It is one of the tumors of the hand in which an irritation is of great importance in its development. Some 70 to 80 per cent of carcinomas develop on the basis of some discernible irritative factor. Only some 20 to 30 per cent of carcinomas of the hand develop without known cause from previously normal skin.

Carcinoma of the hand may be classified etiologically into a number of groups as follows:

1. *Sun and Weather.*—Cancer of the skin of the hand

occurs not infrequently in sailors, farmers, men who spend much of their time out of doors and exposed to wind, rain, and sunshine. Our great Southwest furnishes a great deal of cutaneous carcinoma and, although the face is the most frequent site for these tumors, the hands, especially the dorsum, suffers not infrequently. The lesion starts out as an apparently harmless area of keratosis which later becomes scaly, inflamed, and tends to bleed.

2. *Irradiation with X-Rays and Radium.*—In our experience, the most frequent cause of carcinoma of the hand is x-ray irradiation. It is seen particularly in those individuals whose hands are exposed over a period of months or years to often repeated but small doses of x-ray, either adventitious or therapeutic. Thus we used to see it very often in the older professional roentgenologists who were exposed to irradiation in the days before the dangers were clearly understood. It is still seen occasionally in the roentgenologist, but more often now in doctors who use x-ray in their practice for diagnosis, removal of foreign bodies, insertion of pins, and fracture reduction.

It is also often seen in dentists who up to 10 to 20 years ago were holding films in the patients' mouths while making dental x-ray films. It is seen from time to time in the roentgen and radium technician who for one reason or another has subjected his or her hands to excessive irradiation over a period of years.

We likewise see irradiation carcinoma occurring on the hands of individuals who have been subjected to x-radiation in the treatment of chronic recurring dermatitis of various sorts.

Carcinoma may develop in irradiation dermatitis incurred in other ways as well, but not with the frequency with which it follows chronic repeated small doses.

The majority of these carcinomas are of low grade but if they persist long enough and are subjected to further irritation they eventually metastasize to the regional nodes.

The very great frequency (50 to 60 per cent) with which carcinoma develops in irradiation dermatitis, especially that following frequently repeated small doses, makes excision of all involved skin advisable even in instances in which the patient apparently is keeping the process controlled with salves and oils. Wide excision and immediate grafting is to be counseled early before infection develops in the skin and when carcinoma, if present, is still confined to the skin and held in check by the dense subcutaneous fibrosis which characterizes the condition.

3. *Chemical Irritants.*—These causative factors have long been recognized in various occupations and in industry as leading to the development of carcinoma of the skin. These irritants are many and include acids and alkalis, tar, anilin, pitch, oil, paraffin, grease, paint, and coal soot. True, other parts of the body may be involved as well as the hand, but the hand suffers frequently enough and prophylaxis should be practiced.

4. *Burn Scars.*—Carcinoma has long been recognized as developing in scars of burns, especially of burns which were slow to heal, and are associated therefore with a

## TUMORS OF THE HAND—MASON

thick keloid-like mass covered with a thin and easily traumatized epithelium. It is probably the traumatization of this thin overlying skin which finally leads it to break down into a malignancy. Cracks, infections and possibly even solar irradiation may assist in the process. The carcinomatous breakdown occurs only after many years (40 to 60) following the burn. Here prophylaxis would consist in the removal of these thick keloid burn scars before breakdown has occurred.

5. *Internal Medication*.—Arsenic, taken over a period of many years as Fowler's solution, is well known to lead to the development of keratoses on the palms and soles, and also on other areas of the body. These keratoses are precursors of squamous cell carcinoma, developing in many foci.

6. *Chronic Infection*.—Tuberculosis of the skin, particularly if it has been irradiated, has long been known to break down into carcinoma. Chronic osteomyelitic sinuses likewise may reveal areas of squamous cell carcinoma in the epithelial lining of the sinus tract. Puncture wounds, especially of the palm, have from time to time been reported as leading to carcinoma. It is not always clear whether this is due to foreign body irritation or to infection; or is purely coincidental.

7. *Irritation of Previous Benign Lesions*.—In this category the common wart is the most frequent offender. In some instances it would appear that the lesion was a carcinoma from the start, but in many it seems without question that the preliminary lesion was in fact a wart. Cauterization, the use of escharotics, or irradiation and peeling off with the pocket knife seem to be the most frequent initiatory factors.

8. *No Known Factor*.—Some 20 to 30 per cent of carcinoma of the hand appear without any known previous preceding lesion or causative factor.

Carcinoma of the hand appears usually but not exclusively on the dorsal surface of the hand either as a flat indurated ulcerating lesion, or as a fungating cauliflower-like mass. Its development in areas of x-ray dermatitis cannot always be detected before surgery. The carcinomatous lesions here tend to be harder and more indurated than the lesions elsewhere, they are frequently ulcerative and many are fungating. However, a careful study of skin removed because of irradiation dermatitis, will frequently reveal many foci of carcinoma-in-situ producing little evidence of their presence.

Local invasion and lymphatic involvement may occur quite early in carcinoma of the hand but usually are later manifestations. Seldom does one see a rapidly invasive carcinoma of the hand. Enlargement of the epitrochlear and axillary lymphatics may be due to infection, which is always an element in roentgen dermatitis with carcinoma or any ulcerating or fungating tumors. If regional lymph nodes are enlarged, and at least 50 per cent will be found to be so, they must always be assumed to be involved by carcinoma. In the absence of palpable enlargement and particularly if the tumor is of low grade malignancy, the glands are practically never invaded.

Carcinoma of the hand is almost always squamous cell, but may be basal and is very rarely sweat gland carcinoma.

Treatment consists in wide local removal of the lesion and surrounding skin. Nail bed carcinomata, which tend to be somewhat more malignant than others, are best treated by amputation of the digit. Where local invasion has occurred wide resection must be carried out. It is often possible to carry this out in such a way as to leave functioning elements on the hand, but it occasionally proves necessary to amputate the hand.

The question of lymph node dissection is not always easy to settle. In the early cases of roentgen carcinoma it is not my practice to carry out axillary and epitrochlear dissection as routine. If there is deep extension however, and particularly with bone invasion, lymphatic dissection seems indicated even if the nodes are not palpable. In the presence of palpable nodes, dissection is always indicated. Because of its degree of malignancy one should carefully consider axillary dissection when the nail bed is the site of carcinoma.

Roentgen dermatitis offers a field for the prophylaxis of cancer of the hand. Complete removal of all involved skin and the immediate replacement with split or in early cases free full thickness grafts, rids the hand of this source of danger.

The prognosis is very good for carcinoma of the hand. Statistical studies show cure rates of 40 to 70 per cent.

### Melanoma

The ordinary mole is not often seen on the hand, but if present it should be excised with wide margin. The hand is very subject to trauma and these lesions, if they become malignant following irritation, are so vicious, that they should never be tampered with. They should not be subjected to biopsy by cutting out a section but should be widely removed in their entirety. The use of cautery, electrodisssection, or irradiation is to be deplored.

*Melanomas* of the hand occur most often in the nail bed where they are known as Hutchinson's melanotic whitlow. Unfortunately these are frequently not recognized as melanomas but treated as infection, cancers, exostoses, warts, fungus infection, et cetera. Unfortunately too, they may not be deeply pigmented or may be without pigment although Hutchinson called our attention to the fact that the periphery of the unpigmented lesion is usually black or at least shows evidences of pigmentation.

As melanomas go they represent a better prognosis than any other melanomas, probably because they can be diagnosed early, and because the offending digit is amputated early.

Treatment consists in amputation of the involved finger followed either at once or within three to four weeks by epitrochlear and axillary node dissection.

### Subungual Tumors

Various other subungual tumors which may occasionally be confused with melanoma include carcinoma, glomus tumor, exostosis, warts, fibroma, and in rare instances metastatic tumors.

### Fibrous Tissue Tumors

*Fibromata of the hand* occur in a number of locations including the nail bed. They usually form isolated solitary nodules but occasionally appear lobulated. Sometimes they project as pedunculated mass from the skin. They may be movable or fixed, hard or occasionally soft and are usually painless. They grow slowly and cause trouble only because of size. They may be confused with neurofibromata and vice versa; both on examination and microscopically. They are occasionally found in tendon sheaths or on tendons although here one should be certain the tumor is not actually a xanthoma. Periosteal fibromas have been described. The early nodule in Dupuytren's contracture is often mistaken for a fibroma.

Fibromata do not recur after removal which is usually rather easily accomplished in case of the superficial tumors. The deep ones however, present a problem in dissection.

If there is a recurrence after removal of what appears to be a fibroma on gross and microscopic section, the tumor is probably the so-called recurring fibroma which should probably really belong in the group of sarcomas.

*Fibrosarcomas* present a somewhat perplexing group of tumors variously classified and confused with the neurosarcomas. It is apparent, however, that there are various varieties of fibrosarcomas; some undoubtedly taking origin in connection with nerve sheaths, others with no such apparent association. Some grow with great rapidity, others grow very slowly or not at all for many years and then take on a rapid accession of growth. They may start out as small isolated subcutaneous nodules in the skin (rarely) or in the subcutaneous tissues (more often), or they may take origin very deeply from intermuscular septa and other fascial planes. Other sarcomas may be hard, fixed and painful, and evidence rapid growth with early invasion of blood vessels and pulmonary metastases.

Two main pathologic types are described, the spindle cell and the round cell. Either may be rapidly invasive and prove fatal quite early.

One recurrent fibrous tumor has been noted in an earlier paragraph as a recurring fibroma which might possibly be better classed with the sarcomas. This tumor is usually diagnosed as a fibroma which is not too well circumscribed but which occurs promptly after what appears to be adequate excision. This process continues after successive removals and the diagnosis microscopically will change possibly to neurofibroma or neurosarcoma. The process will eventually require extensive excision and often amputation, although distinct metastases are rare.

As the cellularity increases the tumors become more and more malignant. Early removal of any tumor of the hand is advisable. For the sarcoma, wide excision or amputation offers best chance of cure.

### Lipomas

The *lipomas* are a moderately frequent and usually rather typical tumor of the hand. They form slow-

ly growing, usually well-encapsulated masses either superficially and then often on the dorsum or deep within the tissues where they form indistinct swellings most difficult to diagnose accurately. The superficial ones may be mistaken for epidermoid cysts or even xanthomas but may usually be suspected by their consistency. The deep masses have been divided into the epivaginal or those lying without the tendon sheaths and the intravaginal, those lying within the tendon sheaths. The epivaginal may press upon neighboring structures such as nerves or tendons causing some symptoms or they may infiltrate or push into muscle masses likewise leading to some interference with function. Ordinarily there is little disturbance other than that caused by size or location due to mechanical interference with use of the part by the obstructing mass.

The intravaginal lipomas are unusual and rare tumors which follow the tendon sheaths. They usually appear in the palm where they may be easily mistaken clinically for tuberculous tenosynovitis. Others may lie deep within the muscles, may infiltrate them and produce a very confusing clinical picture seldom diagnosed before operation. These intramuscular lipomas may occasionally lead to rupture of tendons. An occasional one may become malignant.

The removal of the tumor is not difficult in case of the superficial ones. The deep tumors may present difficulties in dissection. The arborescent lipomas may require extremely wide exposure and a careful dissection similar to that required in removal of a tuberculous tenosynovitis. The deep intramuscular tumors may present out-growths resembling the sproutings of potatoes and cannot be simply shelled out. The perineural lipomas may completely bury a nerve which may be easily traumatized in removal.

The prognosis is obviously favorable except in the rare instance of a liposarcoma of which only a few have been reported at any location on the body—the hand being extremely rarely involved.

### Tumors of Joint Capsules and Tendon Sheaths

The tumors taking origin from the joint capsules and tendon sheaths are represented by the most common and by some of the rarest of hand tumors.

The *ganglion* has been intensively studied over the years and its exact nature is still somewhat obscure. Some believe that it is a degenerative process occurring in the dense tissue of joint capsules and tendon sheaths and that it owes its origin to trauma. The traumatic factors leading to its development are thought to be of chronic recurring nature. Those who support this idea point out its frequent occurrence in people who use their hands for frequently repeated motions, e.g., violinists, typists, pianists, et cetera. On the other hand, it is found frequently in people whose hands are not used in this manner. In the early days, when tuberculous tenosynovitis was looked upon as a compound carpal ganglion there was some tendency to ascribe the simple ganglion to tuberculosis. The French authors earlier in the century, prepared a pretty good case for such an assumption, which has no supporters today. The older idea that the ganglion was due to herniation of the synovial

## TUMORS OF THE HAND—MASON

lining of joints and fibrous tendon sheaths is no longer held. Actual communications between joint or tendon sheath and the ganglionic cavity cannot be demonstrated in operation.

King, of Australia, has studied tumors coming from joint capsules and tendon sheaths and his conclusions seem most logical and correlate well with clinical observation. King feels that ganglia are in fact tumors which spring from tissue entering into the formation of joint capsules and tendon sheaths, synovial membranes, and the fibrous tissue about them. King feels it is hardly correct to call them degenerative processes but prefers to look upon them as actual tumors whose product, the cyst (early multiple and late single cystic spaces) is an expression of the cells from which the growth is derived; in other words they are synovial tumors.

Ganglia are seen most often on the dorsal surface of the wrist where they take origin usually from the capsules of the intercarpal joints. They are not infrequently seen in the anatomic snuff box and their deep origin here is in close anatomic relation to the radial artery, which may be damaged during operation for removal. On the volar surface of the wrist they are often seen in the region of insertion of the flexor carpi radialis tendon and the tissue of origin here seems to be the fibrous sheath of the tendon and the underlying joint capsules. Also, at this area, the ganglionic tissue or parts of it may lie deep to the thenar muscles and may escape detection, one explanation for recurrence. Another typical but often not recognized site for ganglia is the fibrous tendon sheath of the flexor tendons over the proximal phalanges. These small pearl-like tumors are frequently mistaken for sesamoid bones. Ganglia are also seen springing from other joints of the hand. The synovial or mucoid cyst of the distal phalanx, to be described below, while similar to ganglion appears to take its origin from the derma rather than joint capsule.

Symptoms of ganglia are largely due to their size and location. They produce cosmetic blemishes, are painful and tender as would be any hard mass in the tissues and may interfere with the use of the hand. The tiny volar digital ganglion at the base of a finger may interfere with grasp. At times, a ganglion may produce symptoms of pain and tenderness of the wrist before a mass becomes evident. Diagnosis may then be difficult. Recurrence after operation may be heralded in by the onset of pain and tenderness after a period of relief from trouble.

Treatment is excision. This is not the simple little operation that it might seem to be. There is no trick in removing the main cystic mass, although this is not easy to accomplish without rupturing it. The difficulty is in following the basal tissue down to its site of origin and removing all of the involved tissue. Tiny cysts may be found scattered throughout the thickened tissues from which the large cyst arises but otherwise the distinction between surrounding normal tissues and tumor is very difficult. Complete removal will entail excision of a segment of joint capsule or fibrous tendon sheath. If this is not done recurrence can be anticipated, and may even take place when a supposedly complete excision has been accomplished. The operation may be done under local anesthesia and should always be done in a bloodless

field secured by the use of a blood pressure cuff. The incision for removal of volar carpal, volar digital and dorsal carpal ganglia should be transverse so as to avoid the contractile scars which are sure to occur following longitudinal incisions.

The wrist or involved digit is splinted for a period of approximately ten days following operation.

Methods of treatment other than operative excision, such as rupturing by a blow, aspiration and injection, carry a high percentage of recurrences.

The *synovial or mucus cyst* resembles very much the ordinary ganglion. It occurs close to the nail at the distal interphalangeal joint and may be mistaken for Heberden's nodes. They differ from ganglia in origin, appearance and behavior. Many appear to be derived from the subcutaneous tissues or the cutis and not from joint capsules. The skin overlying them is very thin and almost translucent so that one can almost see the greyish mucoid contents. They recur after excision with the greatest of rapidity unless excision includes the overlying skin. Pressure of the growth on the nail bed leads to broad grooves on the nail.

Treatment consists in complete excision. Here it is necessary to remove the skin and the tumor, since it appears likely that the tumor may well arise from the lower layers of the derma. The defect thus left must be filled in by a small skin graft. Recurrence is unlikely with this type of removal but is very frequent with less complete procedures in which the skin is saved.

The *xanthoma* (giant cell tumor of tendon sheaths, benign synovioma, et cetera) occurs as an isolated tumor on the hand, occasionally as a manifestation of generalized xanthomatosis. There is some question whether or not this is a true tumor, although actual cholesterol metabolic disturbance is not present in case of the solitary masses as it is in the generalized process.

The histologic pathology of the tumors is typical but variable both from tumor to tumor and from one area of the tumor to another. The tumors are characterized by intermingled areas made up of large multinucleated foreign-body type giant cells, so-called foam cells filled with cholesterol and giving the tumor its yellowish appearance because of the dissolved coloring matter in the cholesterol, areas of spindle shaped endothelial cells and areas with hemosiderin deposition. Various spaces within the tumor which may resemble vascular spaces, are thought to represent synovial spaces. These varying areas are recognizable in the gross specimen by the variably colored lobules (yellow, reddish brown, grey) which present themselves. The tumor is not a sarcoma even though it is often diagnosed as such.

These tumors occur on the volar, lateral, or dorsal surface of the digits, where they form firm evidently encapsulated and lobulated masses which may stretch but do not involve the skin overlying them. They are also seen in the palm or wrist, always in association with joint capsules or tendon sheaths. They are rather firmly attached and do not move on the underlying tissues. They are painless and are not tender, and except for actual size and cosmetic appearance cause little disturbance. They may be confused with the epidermoid cyst although this latter is not lobulated and it is usually possible to palpate lobules in the xanthoma.

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## TUMORS OF THE HAND—MASON

Treatment of the xanthoma is surgical removal which must be done carefully in a bloodless field, both to ensure removal of the entire tumor and to avoid damage to nerves and blood vessels. The digital nerves and vessels will be found to be deeply embedded in between lobules of the tumor to lie flattened and thin on its surface. The tumor is easily recognizable when it is exposed, the areas and lobules of reddish black, yellow, orange, brown and grey are immediately striking. As the tumor is shelled free from its bed the surgeon must be very careful to follow all of its lobular protuberances and to expose and remove every trace. The tumor may be found to take origin from the joint capsule and its site of origin must be excised. Not infrequently a small prolongation of the tumor will be found to penetrate the digital tendon sheath and lobules of the mass must be followed into the sheath and removed.

The prognosis is good since these tumors are always benign but the recurrence rate is likely to be high unless great care is taken to follow and remove every bit of the tumor mass and particularly the basal tissues from which it springs. Very rarely, and then usually only after a number of recurrences, the histology may change and a sarcoma may develop. Occasionally a digit will require to be sacrificed not because of malignancy but because of destruction of blood supply subsequent to the dissection required to remove the tumor growth.

The *synovioma* is a not too uncommon sarcoma springing from tissues of the tendon sheaths, joint capsules and bursae. These tumors are made up of spindle cells with a variable amount of collagen; mitoses are not common. They occur as painless, slow growing masses near joints which are not especially striking at first appearance. When uncovered they may be encapsulated or diffuse, solid or fleshy tumors, occasionally even cystic with areas of hemorrhage or even of butter yellow tissue. They may be very vascular.

The diagnosis may be suspected especially if the origin from joint capsule is determined. The history of injury is occasionally elicited, but the significance is not clear.

It is an actively malignant and metastasizing tumor which promptly recurs after simple excision. Amputation is the treatment of choice.

### Tumors of Blood Vessels

The *vascular* tumors of the hand, as those elsewhere, are relatively frequent. They vary from the simple telangiectatic angiomas to the diffuse and progressive arteriovenous or racemose aneurysms. There is some reason for doubting whether most of them are in fact tumors. Mont Reid from his extensive experience with them, concluded that the majority, if not all, were essentially arteriovenous communications of varying extent and degree. Most of them can be correlated with the various stages of development of the vascular tree, which embryologic study has been so beautifully depicted in the studies of Sabin. Thus we have the angioblastic type, which is made up apparently of cells similar to the primordial angioblastic cells from which the blood vascular system develops. They occur as angioblastic cords, which, by proliferation, may compress normal blood vessels. Other of the tumors are reminiscent of the capillary plexus stage, other of the retiform stage and

still others of the stage of stem formation.

Clinically they are classified into various groups which tend to merge into each other and to be composed of mixed elements of various types.

The *capillary* or *telangiectatic* type occurs as a tiny vascular spot or as the port wine or strawberry nevus. These not infrequently are associated with areas of cavernous tissue to produce sponge-like masses in the subcutaneous tissues or even deeper, covered with telangiectatic skin. These tumors may be destructive by the simple mechanical pressure of their expanding vessels and sinuses but are not malignant. Unfortunately some of these mixed capillary and cavernous tumors may take on the character of arteriovenous aneurysms in later life and spread out over large areas—a good reason for eradicating them early.

The *cavernous* angioma is made up of large vascular sinuses, usually containing venous blood which lie deep to the skin and tend to infiltrate or push aside neighboring tissues. They may extend from volar to dorsal surface of the hand, infiltrate and replace muscles and take over the vascular elements of associated nerves and tendons.

The *arteriovenous* aneurysms frequently involve a certain area of vascular supply such as for example, a digit or several digits. They differ from the traumatic arteriovenous aneurysms in that there are multiple vascular communications throughout the whole involved area. It is not possible to eradicate them by tying a single arteriovenous communication. They form one of the most difficult to treat of all the vascular tumors of the hand.

The capillary and cavernous angiomas are usually amenable to surgery but may require sacrifice of skin and immediate replacement. The capillary type is amenable to x-ray therapy but one is always hesitant to use irradiation on the hand because of the skin damage it may cause. Also, since many of these tumors occur in young people, one would avoid irradiation for fear of the damage which might occur to the growing bones. Injection therapy of the cavernous angioma is recommended by some but I have had no experience of it. Treatment of the arteriovenous (or racemose or cirrhotic) tumors is a very difficult problem. The direct attack upon the tumor mass itself is a most heartbreaking experience. It is practically an impossibility to discover and ligate all or even a fair number of the communications. The structure of the hand is such that searching for them is impossible without absolutely wrecking the hand. One can hardly speak of brilliant success in eradicating the tumor but we have helped these patients the most by measures directed toward diminishing the blood flow to them. Ligation of the arteries in stages combined with partial excision while not perfect seems to offer best chances of help. When a single digit is involved amputation is often the best solution.

The *telangiectatic granuloma*, also known as the pyogenic granuloma, is considered by some to be a true angioma, although others think it is simply granulation tissue tumor of infectious origin. It is seen as a mushroom-like growth of what appears to be granulation tissue. The "stalk" of the mushroom pushes up through a small opening in the epidermis which forms a thin

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collar about the neck of the tumor. Apparently many of these tumors disappear following roentgen therapy, others disappear spontaneously under pressure dressings continued for many weeks. A more certain and rapid method is to excise them and suture the small elliptical defect in the skin. They do not tend to recur.

The *glomus tumor* takes its origin from the neuromyoarterial glomus found as normal heat and circulatory regulating bodies in the skin. These glomi are especially numerous on the hand especially in the nail bed, but are found in varying numbers in practically every area of the body. The glomus or neuromyoarterial glomus is an arteriovenous short circuit found only in warm-blooded animals and is especially abundant in the feet of ducks. Fine arterioles directly connecting with venules form the canal of Suquet-Hoyer. The vessels are surrounded by epithelioid cells which may be modified smooth muscle cells. Many myelinated and non-myelinated nerve fibers are to be found coursing through this structure. The tumor which develops from these bodies evidences the same make-up as the normal glomus and there is some question as to whether this is a true tumor or a hamartoma.

Glomus tumors appear typically in the nail beds where 50 per cent of them are to be found. They appear however in many locations on the extremities, trunk and even rarely on the head and neck. They are usually single, may however be multiple. They are ordinarily 0.5 to 2.0 cm in diameter but occasionally a very large one is found.

They produce a rather typical symptomatology. They develop apparently rather insidiously to produce small painful nodules or painful spot on an extremity usually under a nail where they may be visible as reddish or purplish discolorations. They may change color with temperature change; may be visible at times and invisible at other times. When in the nail bed the overlying nail is raised or rounded so that when the finger is seen "end on" it has a circular shape rather than the semi-circular shape typical of a finger tip.

The area is usually always tender but is more so at some times than at others and as time goes on its periods of sensitiveness increase. Sometimes it is worse in cold weather, at other times warmth makes it worse. Because of the tenderness the patient hesitates to use the digit, keeps it flexed in his palm or keeps his hand in his pocket. Paroxysmal attacks of radiating pain beginning in the tumor pass up the forearm and arm and occasionally even into the neck. A Horner's syndrome has been observed occasionally.

The diagnosis is usually suggested by the typical history and the finding of a tender spot in the area complained of. Occasionally no tumor can be seen, or sometimes warming or cooling of the hand will bring out the color. The rounding of the overlying nail in case of subungual glomus tumors has been noted above. X-ray of such a finger tip will occasionally reveal a depression of the distal phalanx. Similar tender spots may be caused by leiomyomas, and rarely by fibromas and neurofibromas. The amputation neuroma of course should never be confused with the glomus tumor.

Treatment consists in removal of the tumor. They usually shell out quite easily from the surrounding

tissues. The subungual ones require removal of the nail which grows back readily. When operation is carried out under local infiltration anesthesia, the tumor may suddenly pale out as the anesthetic agent is injected, and the tumor may be difficult to locate. Under these circumstances, it resembles a small fibrous tumor.

The glomus tumor does not recur when removed completely and has never been reported to have become malignant.

*Lymphangiomas* are quite rare tumors of the hand, occurring as congenital thickening or soft swelling involving large areas of the hand and forearm. They are of slow growth and are not malignant. It has been advised to excise them, although their usual extent would often make this a difficult procedure.

### Tumors of Bone

*Tumors of the bones* of the hand are not frequent except for the enchondromas. The *enchondroma* is rather typical of the hand, it being seldom seen elsewhere, even in the bones of the foot. The tumor occurs particularly in the shafts of metacarpals or proximal phalanges, never in the carpal bones. They may be multiple and it is usually well to x-ray both hands as well as other parts of the skeleton. In our experience, however, they are almost always solitary.

They develop as slow, usually painless swellings of the shaft of one of the tubular bones of the hand, usually near the head of a metacarpal or base of a proximal phalanx. There may be some dull aching pain to call attention to the tumor, but not infrequently the tumor is first recognized in x-rays taken because of a fracture which has followed rather minimal trauma.

X-ray examination reveals a vesicular area of rarefaction in a fairly well-circumscribed region of the bone. The cortex of the bone will be seen to be expanded and very thin but is intact except in case of fracture. The tumor may resemble a giant cell tumor, somewhat, in x-ray although the latter shows a more soap bubbly appearance.

The enchondroma is benign and requires only thorough curettage. If the patient is seen with a fracture, the fracture is first treated by immobilization on a splint until healing occurs. This follows about the same course of healing as any other fracture, although the cortex remains wafer thin even after healing.

The bone is exposed, preferably where it is thinnest, and after stripping back periosteum for a limited area, the cortex is bitten away over an area large enough to admit a small curet. The pearly white contents of the tumor are then removed. A surprising amount will be found. The surgeon should carefully explore the whole cavity until he is able to bring out no more tumor substance. It is not necessary to fill the cavity thus made with bone chips or a bone graft. It is soon filled with clot which quickly organizes, new bone quickly forms and the thinned-out shaft thickens.

The prognosis is good in that these tumors do not recur if they are thoroughly removed and they are not malignant.

*Exostoses* appear from time to time on the hand, usually in the neighborhood of joints at a point of tendon insertion. They may be multiple. In the x-ray the

## TUMORS OF THE HAND—MASON

tumor appears smaller than gross examination would indicate since they are usually capped with cartilage. They are occasionally encountered in the nail bed, the so-called Dupuytren's subungual exostosis, which pushes up the overlying nail and erodes through it, leading to the development of a granulomatous lesion.

The *osteoid osteoma* was established as a definite entity by Henry L. Jaffe in 1940. It occurs with moderate frequency in the bones of the hand, where Robert Carroll has reported twenty-eight cases from the literature and his own service. Previous to Jaffe's reports, this tumor was confused with other areas of bone rarefaction and sclerosis such as localized osteomyelitis, bone abscess, lues, et cetera. It must still be differentiated from these conditions. It occurs as a small translucent area in the spongy bone or cortex surrounded by denser areas and thickening. The central area or nidus is composed of osteoid tissue about which is found sclerosed bone.

Clinically the tumor is characterized by the development of chronic naggy nocturnal pain which may occur a year or more before the tumor can be recognized in the x-ray. The pain is not severe and usually responds to small doses of aspirin. X-ray examination may have to be repeated from time to time and in various positions, since the tumor can be easily missed, or may not show up in its early stages. It may be mistaken on X-ray examination for abscess, lues, osteochondritis dessicans, xanthoma or even callus. The radiolucent center and associated cortical thickening are the characteristic features.

The tumor, if left alone, may gradually run its course, reach a peak and over a number of years subside as reported by Moberg.

Treatment consists in removal of the tumor mass. The nidus or soft radiolucent center must be removed entirely else recurrence is certain to follow.

*Giant cell bone tumors* do not often occur on the hand. They have been reported in the metacarpals where they develop in the epiphysis as slow growing tumors causing boring pain more severe at night. The appearance in x-ray is fairly characteristic and can usually be differentiated from enchondroma by more definite fine trabeculation. Treatment is surgical removal. Usually the involved bone or section of bone requires removal and may be replaced at once by a bone graft. Curettage of the current-jelly-like contents of the tumor may occasionally prove curative.

*Bone cysts, myxomas, osteomas, bone fibroma and hemangioma* have been described in the bones of the hands. Ewing's tumor may also involve the bones of the hand, as a diffuse process, which may be confused with chronic diffuse osteomyelitis.

*Bone sarcoma* is of great rarity on the hand. Five only are recorded in the literature.

*Metastatic tumors* of the bones of the hand are likewise rather rare but have been reported from primary tumors of the lung, prostate, testis, breast, parotid, endometrium, kidney, colon and adrenals.

### Tumors of Nerves

*Tumors of the peripheral nerves* occur clinically as four different types—isolated nodules (single in 95 per

cent of instances), diffuse spindle-like enlargement of a nerve, plexiform thickening of all the nerves in an area, and as von Recklinghausen's disease.

The *nodular neuromas*, neurinomas or neurofibromas are proliferation of elements of the nerve sheath and usually lie subcutaneously in association with fine rami of sensory nerves. They are usually painless and may be multiple over the whole body. They cause few symptoms and are easily excised without any disturbance of function.

The *fusiform swellings* of a peripheral nerve, in our experience most often affects the median in the lower forearm and wrist, and may extend into the palm and involve the terminal rami of the median in the palm. Although it is said that these tumors often simply expand the nerve which lies spread out and thinned over its surface, in our experience of such tumors such has not been the case. The tumor tissue and the nerve fibers are so inextricably interwoven that it is impossible to separate them and removal of the tumor entails excision of the entire thickened nerve.

The *plexiform neuroma* produces also a thickening of a nerve or group of nerves in an area. However, this thickening extends into the finer branches to the terminal twigs in the skin. The skin itself and the subcutaneous tissues are thick and nodular and there may be gross distortion of a digit or part of a digit or several digits or of the whole hand. This condition is spoken of as *elephantiasis neuromatosa*. Complete removal of all tissue would often lead to severe mutilation which in view of the benign nature of the process is not necessary. The appearance of the hand may be considerably improved, however, by excision often associated with skin grafting.

*von Recklinghausen's disease* is seen involving the hand as it does other parts of the body. Its importance lies in the fact that in about 15 per cent of cases sarcoma develops.

*Neurosarcoma or neurofibrosarcoma* starts usually as a small nodule which promptly recurs after excision. In some instances these recurrences seem to be relatively benign and the surgeon is tempted to carry out rather conservative though wide excision. Some have been followed over a period of many years, eventually requiring amputation. Others, however, are extremely malignant and prove rapidly fatal. The initial operation is the most important one and should be radical and extensive.

### Résumé

In résumé, we have gone over very briefly the tumors of the hand as they have presented themselves. There is a great variety of such tumors, many quite common, others quite rare. About 12 per cent of hand tumors are malignant and of these 90 per cent are squamous cell carcinoma, of which well over half are squamous cell carcinoma developing on the basis of irradiation dermatitis. Irritation of one type or another plays a definite role in the development of tumors of the hand, especially in the case of carcinoma. This fact points toward prophylaxis in this condition. The ease of examination of the hand makes for early diagnosis and early surgery for good prognosis. The anatomic structure of the hand may make adequate exposure and removal difficult.

# Minnesota Academy of Medicine

Meeting of November 11, 1953

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The regular monthly meeting of the Minnesota Academy of Medicine was held at the Town and Country Club on Wednesday evening, November 11, 1953. Dinner was served at 7 o'clock and the meeting was called to order at 8:15 p.m. by the President, Dr. E. A. Regnier.

There were fifty members and one guest present.

In the absence of the secretary, the Minutes of the October meeting were omitted.

Upon ballot, the following men were elected as candidates for membership in the Academy:

Robert Tenner, M.D., Minneapolis

Harold Buchstein, M.D., Minneapolis

Wallace Armstrong, M.D., University of Minnesota

Dr. Ohage moved that, inasmuch as the May meeting of the Academy always conflicts with the Annual Golf Tournament held at the Town and Country Club, the May meeting in 1954 be held at the Minneapolis Club in honor of the present President, and that on alternate years the meetings be held at the Minnesota Club, replacing the regular January meeting. Motion seconded and carried.

The scientific program followed.

Dr. David Anderson, of Austin, then read his Inaugural Thesis on "Non-operative Treatment of Acute Perforated Peptic Ulcer." Lantern slides were shown.

## THE NON-OPERATIVE TREATMENT OF ACUTE PERFORATED PEPTIC ULCER

DAVID P. ANDERSON, M.D.

Austin, Minnesota

The treatment of acute perforated peptic ulcer was considered a settled matter until 1945. It was agreed that the only logical treatment was to operate, and the sooner the better, in order to surgically close the perforation. The few surgeons who performed a gastroenterostomy in addition to closure of the ulcer had been overruled by 1945, because of the increased mortality and the high incidence of late marginal ulcer which followed gastroenterostomy. The advocates of primary gastric resection for the treatment of acute perforated peptic ulcer were in the minority. It was generally accepted and taught that in dealing with an acute perforation of a peptic ulcer, it is the surgeon's duty to save the patient's life, and not to attempt to cure the ulcer. This viewpoint was emphasized forcefully by Dr. Roscoe Graham, whose simple suture technique for the closure of a perforated peptic ulcer was widely used. Significantly, Doctor Graham also demonstrated that peptic ulcer perforations of twenty-four hours' duration or longer hardly needed an operation, except for any such late complications as localized intraperitoneal abscesses. In addition, Doctor Graham offered convincing proof that it was worthwhile to delay operation a few hours, if necessary, to adequately prepare the critically ill, debilitated, or aged patient with an acute perforated peptic ulcer.

Taylor, in 1945, and later Seeley, disturbed the prevailing calm of surgical thought in regard to the treatment of acute perforated peptic ulcer. Prior to the reports of Taylor and Seeley, a few patients here and there had been inadvertently treated non-operatively for acute perforated peptic ulcer, and Wangensteen had given a deliberate non-operative regime some serious thought as early as 1935. However, it was Taylor's report of a

series of selected patients deliberately treated without operation that actually started the new trend of thought on this subject.

Reasoning that a completely empty stomach, like a deflated balloon, will not leak, the advocates of the non-operative treatment of acute perforated peptic ulcer empty the stomach and keep it emptied. The initial soiling of the peritoneum, which is largely chemical rather than bacterial during the first few hours, is treated with antibiotics. Fluids, of course, are administered parenterally and narcotics are used for the relief of pain. Sealing-off of the perforation is left to the natural reparative processes. As all experienced surgeons know, the sealing of a site of perforation does occur quite rapidly, often within a matter of a few hours. If the stomach is kept deflated, the natural reparative processes can be depended upon to firmly seal a perforated peptic ulcer.

Dr. Robert R. Wright of the Austin Clinic treated our first patient by Taylor's non-operative method in April, 1947. Since that time we have treated thirty-seven patients with acute perforated peptic ulcer by the non-operative method. We have been so favorably impressed with the advantages of this method over the operative management that we believe a report of our experiences is justified.

### Criteria for Accepting the Diagnosis of Acute Perforated Peptic Ulcer in Patients Treated Non-Operatively

The statement that we have treated thirty-seven patients with acute perforated peptic ulcer by the non-operative

## ACUTE PERFORATED PEPTIC ULCER—ANDERSON

regime cannot be accepted as a statement of fact without further proof. It is a fact, attested by the records of the patients reported, that a final diagnosis of "acute perforated peptic ulcer" was made for each patient, and the results of the treatment are a matter of record. It remains to be proved that these patients did, in fact, have acute perforated peptic ulcer rather than some illness simulating this disease. Direct proof of the actual existence of an acute perforated peptic ulcer, such as one can obtain at operation, is naturally not available in patients treated non-operatively. It behooves us, therefore, to be very strict in selecting patients, who were treated without operation, that we report as having had acute perforated peptic ulcer. So-called "perforating" or "penetrating" peptic ulcers must be excluded, as well as other diseases which commonly simulate acute perforated peptic ulcer.

We feel that there is no reasonable doubt that twenty-three of the thirty-seven patients diagnosed as "acute perforated peptic ulcer" did, in fact, have the disease. Each of these twenty-three patients fulfilled the following rigid standards that we have established for ourselves as proof of the actual existence of a frank, acute perforated peptic ulcer in patients treated non-operatively:

1. A clear-cut clinical history of acute, severe abdominal pain.
2. Physical findings of diffuse, board-like rigidity of the abdomen; tenderness; and rebound tenderness.
3. X-ray proof of a gastric or duodenal ulcer *with an active crater*.
4. Absence of early or late evidence of other diseases which might simulate acute perforated peptic ulcer.

The treatment of each of these twenty-three patients considered to have proved acute perforated peptic ulcer was supervised by the author, or one of his surgical associates in the Austin Clinic. Confirmation of the clinical and x-ray diagnosis was aided by other relevant findings:

1. Twenty-two of the twenty-three patients had definite peptic ulcer symptoms for a few days to several years prior to the onset of the acute abdominal catastrophe. Fifteen of these had definite x-ray proof of chronic peptic ulcer.
2. Eight of sixteen patients on whom an upright or left lateral decubitus x-ray was done had free gas in the peritoneal cavity. Only 5 per cent had free gas.
3. Three patients in this group have had late elective operations for peptic ulcer (gastric resection or gastro-enterostomy with vagotomy) performed by the author. Seven others have received medical treatment at the Clinic for recurrent peptic ulcer.

We have classified the remaining fourteen patients, who were diagnosed "acute perforated peptic ulcer" and treated non-operatively, as "*probable*" acute perforated peptic ulcer. We feel that an unequivocal diagnosis cannot be made in this group because of lack of personal observation of the patient, or because of lack of late x-ray evidence of an active peptic ulcer. However, each of the fourteen patients presented findings that were considered a typical picture of an acute surgical abdomen,

TABLE I. FINAL CLASSIFICATION OF FIFTY PATIENTS WITH DIAGNOSIS OF ACUTE PERFORATED PEPTIC ULCER

23	"Proved"	cases treated non-operatively.
14	"Probable"	cases treated non-operatively.
1	Patient, initially treated non-operatively, operated on after seven hours.	
2	Patients operated on initially.	
5	Patients, treated non-operatively, reclassified as having "perforating" or "penetrating" peptic ulcer.	
5	Patients, treated non-operatively, reclassified as having "other diseases."	

presumably due to an acute perforated peptic ulcer. Operation ordinarily would have been advised for these patients.

In order to rigidly re-examine our evidence, we have reviewed the records of all patients with the final diagnosis, "acute perforated peptic ulcer," who were treated in the St. Olaf Hospital, Austin, during the period of this study (April, 1947, to October, 1953). There were fifty patients so diagnosed during this period. A final classification of the diagnosis in these fifty patients is given in Table I. This was made after re-evaluation of the hospital record, late x-ray examinations, and the patient's subsequent medical course.\*

### Method of Treatment

Our method of non-operative management of acute perforated peptic ulcer follows the basic principles outlined by Taylor, Seeley, and others who have pioneered this treatment. Certain minor modifications have been made. The regime is as follows:

1. *The stomach is completely emptied and kept empty.*—Emptying of the stomach, of course, is absolutely essential. We have found that an ordinary Lavin tube is satisfactory for the initial aspiration of the stomach, as well as for the continuous gastric suction. The stomach is thoroughly irrigated with sterile normal saline and aspirated until we are certain that it is empty. Continuous gastric suction is then maintained for forty-eight to seventy-two hours, or longer, until any abdominal distention has been relieved, peristalsis is active, and all signs of peritoneal irritation have subsided. Extreme care is taken to be certain that the stomach tube is patent and functioning properly at all times.

After forty-eight to seventy-two hours, the stomach tube is clamped, but left in place, and oral feedings of two ounces of milk and two ounces of water are given every two hours while the patient is awake. The stomach contents are aspirated two hours after the oral feedings and the residual gastric content recorded. If the residual stomach contents are less than an ounce

\*Several hospital staff members who are not associated with the Austin Clinic have adopted the non-operative management of acute perforated peptic ulcer. The author wishes to express his appreciation to these men for the courtesy of being informed of or seeing their patients during the course of treatment: Drs. P. C. Leck; P. A. Lommen; C. L. Sheedy and Leo Twiggs.

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on repeated aspirations during a twelve-hour period, it is assumed that there is no pyloric obstruction and the Levin tube is removed. If pyloric obstruction persists, the stomach aspirations are continued until it subsides. After the Levin tube is removed the patient is placed on the usual medical regime for the management of an active duodenal ulcer. A stomach x-ray can be done safely, with a little caution on the part of the roentgenologist, on the seventh to tenth day.

2. *Narcotics are used for the relief of pain.*—Surprisingly, many of the patients in this series, who were admitted to the hospital with intense pain, required no narcotics after the first twelve to twenty-four hours of non-operative treatment.

3. *Parentral fluids are administered until oral intake is adequate.*—The average patient requires parenteral fluids for the first two to four days only.

4. *Antibiotics are administered prophylactically, usually for five days.* A combination of 300,000 units of penicillin and 0.5 grams of streptomycin, administered twice daily, has been our favorite.

5. *Careful observation at four- to six-hour intervals* is mandatory during the first twelve to twenty-four hours. This observation should be conducted by a surgeon familiar with the management of an acute surgical abdomen. The surgeon should keep an open mind during this early period and be willing to reverse his opinion and recommend operation if progress is not satisfactory. We have made it a practice to inform the patient, his relatives, and the referring physician that the election of non-operative management is not final, but is subject to change after a preliminary period of observation.

Usually, after four to six hours, and almost invariably within the first twelve hours, the patient with an acute perforated peptic ulcer shows definite signs of improvement. Progression of symptoms or failure to improve during the early period of observation is considered an indication for surgical intervention.

### Results of Treatment

The twenty-three patients classified as "proved" acute perforated peptic ulcer all recovered on a non-operative regime. There was only one complication in this group: a localized pelvic abscess which responded promptly to transrectal drainage.

One patient, placed on a non-operative regime by the attending physician, was operated on by the author after an initial observation period of seven hours. Operation was elected for the following reasons:

1. Lack of adequate response during a seven-hour period of observation.
2. The presence of barium in the stomach.
3. The presence of a known high-grade pyloric obstruction.

At operation a large pre-pyloric perforated ulcer was found. The perforation, which was 1 cm. in diameter, was completely sealed by omentum and there was little or no soiling of the peritoneum. A subtotal gastric resection was elected as the procedure of choice. The patient's recovery was entirely uneventful (Case 1).

*Case 1.*—P. C., male, aged sixty-five, was admitted to the hospital because of severe pain following stomach x-ray which showed pyloric obstruction.

*Course.*—A Levin tube was inserted on admission by the attending physician. The tube was irrigated "several times" with soda solution, but it did not work well. Suddenly, severe abdominal pain developed fourteen hours after admission. The surgical consultant was called seven hours after onset of the pain.

*Treatment.*—An operation was elected because of: (1) pyloric obstruction, (2) presence of barium in the stomach, (3) difficulty in emptying the stomach with the Levin tube.

*Operation.*—A chronic pre-pyloric gastric ulcer with perforation 1 cm. in diameter was found. Perforation was sealed by omentum. Subtotal gastric resection was done. The recovery was uneventful.

Twelve of the fourteen patients diagnosed clinically as acute perforated peptic ulcer, and classified by us on review as "probable" cases, recovered without complications when treated non-operatively. *Two patients in this group died.* One of these patients was an eighty-five-year-old woman who died in the hospital after complete recovery from peritonitis which was presumably due to acute perforated peptic ulcer. Death was due to cerebral arteriosclerosis and arteriosclerotic heart disease with cardiac decompensation (Case 2).

*Case 2.*—L. S., female, aged eighty-five, had a history of a duodenal ulcer for many years. She had an inactive ulcer with complete pyloric obstruction operated on five years previously (pyloroplasty). She was admitted to the hospital with an acute epigastric pain of three days' duration.

*Findings.*—Generalized peritonitis, free gas beneath diaphragm, pneumonia; arteriosclerotic heart disease, and glaucoma were found.

*Treatment.*—A non-operative treatment was decided upon.

*Course.*—The patient recovered from peritonitis. She tolerated soft foods and had no abdominal distress for five weeks prior to death from arteriosclerotic heart disease with cardiac decompensation.

The patient expired forty-seven days after admission. No autopsy was performed.

The second death was that of a seventy-nine-year-old man who was admitted to the hospital with a massive hemorrhage from a chronic duodenal ulcer. Probably perforation occurred as a terminal event and was a definite factor in the patient's death (Case 3).

*Case 3.*—H. S., male, aged seventy-nine, had a history of duodenal ulcer for many years. He had epigastric pain and tarry stools for two weeks. The hemoglobin was 46 per cent. He had arteriosclerotic heart disease and auricular fibrillation.

*Treatment.*—He received transfusions and a special diet for seven days. Improvement was noted. The hemoglobin was 100 per cent.

*Course.*—Vomiting of undigested food and blood, with increased pain, started the eighth hospital day. A Levin tube was inserted on the tenth day for "gastric dilatation." Fecal impaction was noted. There was tenderness and rigidity in upper abdomen.

The patient expired on the thirteenth hospital day from anuria, cardiac failure and peritonitis. An autopsy was not obtained.

## ACUTE PERFORATED PEPTIC ULCER—ANDERSON

It is necessary to attribute this death statistically to the non-operative method of management, although there is a question as to the accuracy of the diagnosis. It should also be noted that the non-operative management was not ideal; that there were serious associated diseases; and that two surgical consultants felt that the patient would not tolerate even the simplest operative procedure.

The two patients operated on initially and the ten patients, treated non-operatively as acute perforated peptic ulcer but reclassified by us as "penetrating ulcers" or "other diseases," all recovered without serious complications.

### Hazards of Non-Operative Treatment

The deliberate non-operative management of acute perforated peptic ulcer has certain potential hazards that should be forcefully stressed.

1. *Errors of diagnosis.*—An erroneous diagnosis of acute perforated peptic ulcer, when accompanied by a decision to treat the patient non-operatively, is a very real danger of this method of therapy. Some surgeons argue that this danger is so great that they will not consider the use of the non-operative regime under any circumstances.

We feel that an accurate diagnosis is possible in most instances, and that with certain safeguards, a brief delay for observation is not detrimental. On many occasions during the period covered by this report, we have considered the possibility of an acute perforated peptic ulcer in the differential diagnosis of an acute surgical abdomen. When operation was deliberately delayed for a few hours of observation, the correct diagnosis and proper course of treatment often became amazingly clear, and the patient benefited thereby. A necessary operation was delayed unduly because of the erroneous diagnosis of acute perforated peptic ulcer on only one occasion. This patient's history is summarized briefly in Case 4.

**Case 4.**—I. H., male, aged fifty-six, was known to have a duodenal ulcer with recent active symptoms. He was admitted to the hospital with severe abdominal pain of four hours' duration, shock and board-like rigidity. White blood count was 20,000. An x-ray of the abdomen showed no abnormalities.

*Course.*—In six hours the patient was not improved. After twelve hours the pain was more severe, his condition was worse, the board-like rigidity were unchanged. After forty-eight hours the patient was toxic; the abdomen was tense and distended. On the third to seventh day he was improved; an LLQ mass developed.

*Operation.*—Abdomen was explored on the seventh day after I & D revealed old bloody fluid. Volvulus of ileum with seventeen feet of gangrenous bowel, resection of ileum.

The patient expired two and one-half months after the operation with a fecal fistula, toxic hepatitis, and uremia.

This one incident forcefully emphasizes, in the breach thereof, a firm rule that we have established in the non-operative management of acute perforated peptic ulcer:

*Re-evaluation after two to four hours of non-operative management is mandatory. If the patient is not improved, or if the diagnosis is in doubt after four hours, operation is indicated.*

The initial election of non-operative therapy is not final, but is subject to change after a preliminary period of observation. We failed to follow this rule in the management of the patient discussed above. On two other occasions, we have evoked this rule when we operated on a known perforated pre-pyloric ulcer that was not improving, as cited above, and once when we operated on a suspected acute perforated peptic ulcer, after a preliminary period of observation, because of persisting pain and a change in the physical findings.

**Case 5.**—R. G., male, aged fifty-seven, was admitted to the hospital with severe abdominal pain of six hours' duration with board-like abdominal rigidity. The hemoglobin was 40 per cent. The patient had a history of indigestion and increasing weakness for one year. X-ray examination of the abdomen gave negative findings.

*Treatment.*—Gastric suction; transfusions and narcotics. General condition improved, but pain was severe, abdomen rigid and LLQ mass suspected after six hours' observation. An operation was advised.

*Operation.*—Leiomyosarcoma of jejunum 5 inches in diameter, with gross perforation and hemorrhage, was found. Resection was performed. The patient recovered.

2. *Improper management.*—Another potential hazard in the non-operative management of acute perforated peptic ulcer is the danger of poor supervision of the treatment. The simplicity of the method is likely to create a false sense of security until the physician learns, too late, that things are not going well. It must be understood that the non-operative regime is an active, dynamic method of treatment. It should *not* be entrusted to anyone who is not thoroughly familiar with the diagnosis and treatment of the acute surgical abdomen. It should *not* be elected as the treatment of choice unless the surgeon is willing to give the patient the same careful supervision that he would give a critically ill postoperative patient. The surgeon must know that the stomach is empty, and he must know that it will be *kept emptied* by the surgical personnel under his supervision. He must observe the patient carefully, and he must be willing to change his course of therapy if the indications arise.

### Contraindications to Non-Operative Management

The following may be considered as *absolute* contraindications to the non-operative management of acute perforated peptic ulcer:

1. *An uncooperative patient.* An alcoholic, demented or uncooperative patient who will not leave the Levin tube in place should not be treated by this method. Complete and continuous emptying of the stomach is absolutely essential to the success of the treatment.

2. Perforation when the stomach is filled with barium should not be treated non-operatively for fear of chemical peritonitis due to barium, which is difficult to remove from the stomach with gastric suction.

(Continued on Page 622)

# In Memoriam

## GUSTAF EDLUND

Dr. Gustaf Edlund of Saint Paul, widely known as a physician and golfer, collapsed and died suddenly at his home, 3122 Owasso Boulevard, Saint Paul, June 10. He was sixty-two years old and, according to his family, had never been ill before in his life.

Dr. Edlund had practiced medicine and surgery for thirty-three years in Saint Paul with offices at 120 North Snelling Avenue. He was a former president of the Midland Hills Country Club and was a member in recent years of the North Oaks Country Club. He was said to have shot holes-in-one at least three times in a long golfing career which began in boyhood.

He was born in Saint Paul and received his advanced education at the University of Minnesota and Northwestern University in Chicago from which he received his medical degree in 1920. He served his internship at Miller Hospital and was a member of the professional staffs at Gillette State Hospital and Midway Hospital in Saint Paul.

Dr. Edlund was a member of the Ramsey County Medical Society, the Minnesota State Medical Association and the American Medical Association. He was also a member of Osman Temple of the Shrine and the Reformation Lutheran Church in Saint Paul.

Survivors are his wife, Helen; a son, Gustaf, Jr.; three brothers, John and Edward of Saint Paul and Fred of San Francisco; two sisters, Esther of Saint Paul and Elsie of Minneapolis.

## FREDERICK WILLIAM ENGDAHL

Dr. Frederick W. Engdahl died unexpectedly of a heart attack at his home in Dallas, Texas, June 11. Until about twelve years ago, Dr. Engdahl had practiced at Ortonville with Doctors Charles Bolsta, B. R. Karn and D. M. O'Donnell. He was sixty-three years old.

Son of the Rev. and Mrs. A. Engdahl of Ortonville, Dr. Engdahl was born in Milbank, South Dakota, but went to school in Ortonville and then graduated in civil engineering from the Cincinnati, Ohio, University. He served for some years as highway engineer for Big Stone County before going to the University of Minnesota to study medicine. He served his internship at St. Mary's Hospital in Duluth and practiced at Mankato and Grand Rapids before going to Ortonville. He was a veteran of World War I and a member of the Minnesota State Medical Association and the American Medical Association as well as the West Central Minnesota Medical Society.

Surviving are his wife, the former Ruth Rishoff; a daughter, Mary Elizabeth, and son, Frederick W., Jr., both of Dallas; one brother, Theodore M. of Los Gatos, California; and two sisters, Mrs. C. A. Zweiner, Saint Paul, and Mrs. Luther Youngdahl, wife of Judge Luther Youngdahl, Washington, D. C.

## CHARLES GEORGE FORREST

Dr. Charles G. Forrest died June 17 at the age of eighty-eight in his home at Clearbrook. He had been in virtual retirement for some years after more than forty years of active practice spanning the "horse and buggy days" at Clearbrook.

Dr. Forrest was born at Lake City and attended Pillsbury Academy in Owatonna before going to the University of Minnesota from which he was graduated in medicine in 1899. He practiced for a short time in Bagley before moving to Clearbrook in 1910 and had been honored as an outstanding citizen and civic leader, as well as beloved family doctor, by the community.

In 1949, Dr. and Mrs. Forrest had been chosen by the Minneapolis Aquatennial committee from hundreds of nominees as the "happiest couple in Minnesota." They were feted guests of the Aquatennial that year and received a trip to California as part of the celebration. At that time it was estimated that Dr. Forrest had delivered more than 3,000 babies during his long and eventful career as a country doctor and he had found time, also, to serve for forty years on the Clearbrook school board, and to act as local health officer and as a director of the First State Bank of Clearbrook. He maintained an active interest in church work, too, and kept an eye on the nearby Red Lake Indian reservation where he had many Indian friends.

In 1901, Dr. Forrest married Miss Rosetta Nichols, a teacher in the Bagley school, who survives him. Other survivors are a daughter, Mrs. George Hoppe of Seattle; and three foster daughters, Mrs. Henry Dahlberg of Clearbrook, Mrs. Frank Gambucci of Hibbing and Mrs. Nicholas Faymoville of Minneapolis. There are eight grandchildren.

## ARNOLD PHILLIP GRUENHAGEN

Arnold Phillip Gruenhagen, Saint Paul surgeon, died after a long illness, July 6, at St. Luke's Hospital in Saint Paul. He was fifty-nine years old.

Dr. Gruenhagen was born at Shell Lake, Wisconsin, but came to Saint Paul as a child and received his preliminary education there. He took a B.S. degree from Hamline and the University of Minnesota and was graduated in medicine from the University of Illinois. After an internship and residency at Ancker Hospital in Saint Paul, he became associated in practice with the late Dr. A. E. Comstock and joined the staffs of Miller, Ancker and St. Luke's hospitals, becoming chief of staff at St. Luke's Hospital later. He served as a member of the teaching staff of the University of Minnesota medical school for fifteen years, and for twenty years he was a teaching staff member of Ancker Hospital.

Among his professional affiliations was membership in the American College of Surgeons of which he was a fellow, the American Medical Association, the Minne-

## IN MEMORIAM

sota State Medical Association and the Ramsey County Medical Society. Also, he was a member of the Saint Paul Surgical Society, Alpha Kappa Kappa medical fraternity, Rotary and the Town and Country Club.

Dr. Gruenhagen had been ill and retired from practice for more than seven years. He is survived by his wife, the former Floy Brown; his mother, Mrs. Charles Zieman of Saint Paul; and one sister, Mrs. Langdon D. Strong of Milwaukee.

### JAMES FELTON HAMMOND

Dr. J. Felton Hammond of Saint Paul, died August 10, 1954, at the age of seventy-two. He had practiced at the same location in the Lowry Medical Arts Building since 1910 and was a life member of the Minnesota State Medical Association and the Ramsey County Medical Society. He was found dead of a heart attack in his car in the garage at the rear of his home.

Dr. Hammond was born at Ironside, Quebec, Canada, and attended Ottawa Collegiate Institute and McGill University, from which he received his medical degree in 1906. After serving an internship at Montreal Maternity Hospital, he spent two years in postgraduate work at the Montreal General Hospital and the Alexandria Hospital in Montreal before coming to Saint Paul to specialize in obstetrics and gynecology in 1910. He had been an instructor in obstetrics and gynecology at the University of Minnesota and was a staff member at Ancker, St. Luke's and Miller Hospitals in Saint Paul. He was a member of the Minnesota Academy of Medicine as well as of Ramsey County Medical Society, the Minnesota State Medical Association and the American Medical Association.

Dr. Hammond is survived by his wife, Eleanor Jane, and four sisters and two brothers who live in Canada.

### MELVIN S. HENDERSON

Dr. Melvin S. Henderson, founder of the section of orthopedic surgery at the Mayo Clinic, president in 1932 of the Minnesota State Medical Association and former associate of Drs. W. J. and C. H. Mayo, died at his home in Rochester, Thursday, June 17. He had retired from active association with the Clinic in 1948 and was seventy-one years old at the time of his death.

When Dr. Henderson went to Rochester as a young man just out of medical school and the University of Toronto, there were only three special sessions in the Mayo Clinic; one was for diseases of the eyes, one for diseases of the ear, nose and throat and one for genito-urinary diseases. Following a year's internship at Ancker Hospital in Saint Paul (then the City and County Hospital) in 1907, he went to the Clinic and was given charge, at first, of the outpatient post-operative department. Soon he became first assistant to Dr. W. J. Mayo and, in 1910, he formed the first section devoted exclusively to orthopedic surgery. There were few such specialized sections anywhere at the time and Dr. Henderson was his own brace-maker until he could pick and train a man to undertake this exacting auxiliary to orthopedic surgery.

Subsequently he spent considerable time in Liverpool with the celebrated Sir Robert Jones and at Edinburgh and London studying the new specialty and became, him-

self, one of the most celebrated orthopedic surgeons in the world.

Dr. Henderson was born in Saint Paul, son of Mr. and Mrs. Melvin Brooks Henderson, and it was Dr. Archibald MacLaren of Saint Paul who gave him the letter of introduction which brought him to the attention of the Doctors Mayo.

He was an associate and then professor of orthopedic surgery in the Mayo Foundation Graduate School of the University of Minnesota until 1951. He was a member of the Board of Governors of the Mayo Clinic from 1924 to 1947 and vice chairman of the board from 1937 to 1946. He served as chairman of the executive committee of the Mayo Clinic from 1918 to 1920, and from 1937 to 1950 he was a member of the board of the Mayo Association.

Among many professional affiliations and honors, he was president of the Board of Orthopedic Surgery in 1934 and president of the American Orthopedic Association in the same year. Later he was elected president of the American Academy of Orthopedic Surgeons. Besides serving as president of the state medical association he was also president of the Southern Minnesota Medical Association, a member of the Olmsted-Houston-Fillmore-Dodge County Medical Society, the American Medical Association and a large number of other national and international organizations.

Dr. Henderson is survived by his wife, the former Mabel Christensen and two sons, Dr. Edward D. Henderson, a member of the section at the Mayo Clinic which his father founded, and Melvin Starkey Henderson, also of Rochester.

### IRVING WILLIAM STEINER

Dr. I. W. Steiner of Winona, age sixty-six, died at Winona General Hospital after a short illness May 4, 1954. He was a former Winona County coroner, the former secretary for many years of the Winona County Medical Society and he had practiced medicine and surgery in Winona for thirty-five years.

Dr. Steiner was born at Independence, Wisconsin, and had his secondary education there and at Arcadia, Wisconsin. After two years at the Armour Institute in Chicago he entered pre-medical training at the University of Chicago and was graduated in medicine from Rush Medical School. After a year's internship at Presbyterian Hospital in Chicago he entered practice at Harvey, Illinois, and, a year later, joined the armed forces for service in World War I. He went to Winona immediately after the war to engage in general practice there.

Dr. Steiner served as coroner from 1923 to 1927 and joined the State Guard as major in the Ambulance Corps during World War II. He was vice president of the Minnesota Chapter of the American Academy of General Practice, a member of the American Medical Association, the Minnesota State Medical Association and the Southern Minnesota Medical Association. He was also a member of Rotary and a 32nd degree Mason as well as a member of the Elks, the American Legion, the Winona Athletic and Country

## LETTERS TO THE EDITOR

Clubs and St. Paul's Episcopal Church in Winona. He was a staff member of Winona General Hospital.

Surviving are his wife; a daughter, Susan of Winona; and one sister, Mrs. Donald Ruhnke of Canton, Ohio.

### JOSEPH J. STRATTE

Dr. Joseph J. Stratte, formerly of Hallock, died suddenly in Minneapolis, April 9, while attending a continuation study course on urology at the Center for Continuation Study on the University campus. He was sixty-seven years old.

Dr. Stratte had practiced in Grand Forks, North Dakota, since 1932. He was born in Dawson, Minnesota, received his medical education at the University of Minnesota and served his internship at the University Hospital. He became assistant to the chief of surgery at the University in 1918 and opened his practice in Hallock in 1922. He remained a staff member at the Kittson Memorial Hospital at Hallock and he had just completed a term as chief of surgery at Deaconess Hospital in Grand Forks.

He was a member of the Minnesota State Medical Association until 1932 when he transferred his membership to the Grand Forks District Medical Society and the North Dakota State Medical Association. He was also a member of the North Dakota-Manitoba Urological Society.

Survivors include his wife, the former Irene Dille; four children by an earlier marriage, Dr. John Stratte, Enumclaw, Washington, Dr. Paul Stratte, Redding, California, Mrs. B. M. Griffin, Mauston, Wisconsin, and Mrs. E. L. Billing, San Francisco; a brother, Henry Stratte, Dawson; a sister, Mina Stratte, Glendale, California, and ten grandchildren.

### MERRITT WHITACRE WHEELER

Dr. Merritt W. Wheeler, sixty-seven years old, died at his home in Stillwater, June 21. He had practiced medicine in Saint Paul for twenty-eight years until his retirement in 1946.

Dr. Wheeler was born at Albion, Iowa, and received his B.A. and B.S. degrees from Iowa Teachers College and the University of Iowa, respectively. His medical education was obtained at the University of Minnesota. After an internship of three years at St. Joseph's and St. Luke's Hospitals in Saint Paul he took one year's post-graduate training at Tulane University and practiced for six years at Glencoe. Following service as captain in the Army Medical Corps in World War I he moved to Saint Paul and, after a few years, limited his practice to eye, ear, nose and throat work.

Dr. Wheeler was a member of the Ramsey County Medical Society, the Minnesota State Medical Association and the American Medical Association. He was also a member of the American College of Surgeons, the American Legion, Veterans of Foreign Wars, Rotary, Hard-of-Hearing League and Masonic order.

Surviving are his wife, Ruth; a son, Merritt W., Jr., of Lake Elmo; a daughter, Mrs. Henrietta Glenn of Saint Paul, wife of Municipal Judge Andrew Glenn; a sister Mrs. Myrl Gardner of Saint Paul; a brother, Forrest of Minneapolis, and four grandchildren.

## Letters to the Editor

Dear Editor:

Because of the great demand on the part of physicians to have a complete set of the Society's monograph series for the practicing physician, National has reprinted copies of all of them.

We are now in a position to fill requests from physicians who may not have received these publications when they were originally distributed.

Is there any possibility of including this announcement in one of the publications of the MINNESOTA MEDICINE?

The complete list of monographs now available is as follows:

1. THE CANCER PROBLEM, by Dr. Shields Warren, 1948.
2. CANCER OF THE HEAD AND NECK, by Dr. Hayes Martin, 1949.
3. THE DIAGNOSIS OF GENITO-URINARY NEOPLASMS, by Dr. Victor F. Marshall, 1949.
4. CANCER OF THE LUNG, by Dr. Richard H. Overholt and Dr. Sherman W. Atwell, 1950.
5. CARCINOMA OF THE BREAST, by Dr. C. D. HAAGENSEN, 1950.
6. CANCER OF THE ESOPHAGUS AND THE STOMACH, by Dr. Owen H. Wangensteen, 1951.
7. VALUE OF EARLY DIAGNOSES OF MALIGNANT LYMPHOMAS AND LEUKEMIAS, by Dr. Lloyd F. Craver, 1952.
8. CANCER OF THE FEMALE GENITAL TRACT, by Dr. Herbert F. Traut and Dr. Ralph C. Benson, 1954.

These monographs are available without charge. Requests can be addressed to: Minnesota Division, American Cancer Society, 295 North Snelling Avenue, Saint Paul 4, Minnesota.

Sincerely yours,

GLORIA FERNANDEZ

Education Director, Minnesota Division  
American Cancer Society

May 23, 1954

When I came to consider local government, I began to see how it was in essence the first-line defense thrown up by the community against our common enemies: poverty, sickness, ignorance, isolation, mental derangement and social maladjustment. The battle is not faultlessly conducted, nor are the motives of those who take part all righteous or disinterested, but the war is, I believe, worth fighting, and this corporate action is at least based upon the recognition of one fundamental truth about human nature: we are not only single individuals, face to face with eternity and our separate spirits; we are members one of another.—WINIFRED HOLTY, "South Riding," quoted in European Conference on Health Education of the Public, London, England, April 10-18, 1953.

# ♦ Reports and Announcements ♦

## MEDICAL MEETINGS

### National

American Cancer Society, Board of Directors and special committee meetings, Hotel Radisson, Minneapolis, Minnesota, June 2, 1954.

American Heart Association, Washington, D. C., September 12-17, 1954.

Annual Assembly in Otolaryngology, University of Illinois, Chicago, Illinois, September 6-11, 1954.

Annual Convention of the National Society for Crippled Children and Adults, Hotel Statler, Boston, Massachusetts, November 3-5, 1954.

Industrial Health Conference Seventh Annual, Shamrock Hotel, Houston, Texas, September 23-25, 1954.

### International

Conference of International Union Against Tuberculosis, Madrid, Spain, September 26-October 2, 1954.

Congress of International Association for the Prevention of Blindness, New York, New York, September 12-17, 1954.

International Anesthesia Research Society, Los Angeles, California, October 10-14, 1954.

International Congress of Clinical Pathology, Washington, D. C., September 6-10, 1954.

International Congress of Diseases of the Chest, Barcelona, Spain, October 4-8, 1954.

International Poliomyelitis Congress, University of Rome, Orthopedic Clinic, Rome, Italy, September 6-10, 1954.

International Congress of Hematology, Paris, September 6-11, 1954.

International Society of Blood Transfusion, Paris, France, September 12-19, 1954.

International Congress of Industrial Medicine, Naples, Italy, September 13-19, 1954.

International Congress of Internal Medicine, September 15-18, 1954.

International Congress of Ophthalmology, University of Montreal and McGill University, Montreal, Canada, September 9-11, 1954.

International Congress of Orthopedic Surgery and Traumatology, Berne, Switzerland, August 30-September 3, 1954.

International Society of Geographical Pathology, Washington, D. C., September 6-10, 1954.

World Congress of Cardiology, Washington, D. C., September 12-18, 1954.

World Medical Association, Rome, Italy, September 26-October 2, 1954.

## NORTHERN MINNESOTA MEDICAL ASSOCIATION

The annual meeting of the Northern Minnesota Medical Association will be held at Willmar, Minnesota, Friday and Saturday, September 10 and 11, 1954. The program will include the following features:

### Friday, September 10

*Morning Session—10:00 A.M.*

"Fractures of the Elbow"—WESLEY BURNHAM, M.D., Minneapolis

Discussion

"Pruritus Ani"—H. M. FRYKMAN, M.D., Minneapolis

Discussion

"Premature Separation of the Placenta"—BRUCE WILLIAMS, M.D., Duluth

Discussion

*Business Meeting—11:50 A.M.*

*Luncheon—12:30 P.M.*

Hosts—Kandiyohi-Swift-Meeker County Medical Society

*Afternoon Session—2:00 A.M.*

"Rheumatic Fever"—ROBERT A. GOOD, M.D., Minneapolis

Discussion

"The Modern Trends in the Management of Hypertension"—ARTHUR C. KERKHOF, M.D., Minneapolis

Discussion

Panel Discussion:

"The Management of the Bleeding and Recurrent Peptic Ulcers"—OWEN H. WANGENSTEEN, M.D., Minneapolis; GEORGE A. HALLENBECK, M. D., Rochester; J. J. COLL, M.D., Duluth

*Annual Banquet—7:00 P.M.*

Address: PAUL DE KRUIF, Holland, Michigan

### Saturday, September 11

*Morning Session—9:00 A.M.*

Clinico-Roentgen-Pathological Conference—Conducted by

H. G. MOEHRING, M.D., Duluth

## MINNESOTA ACADEMY OF OCCUPATIONAL MEDICINE AND SURGERY

The Minnesota Academy of Occupational Medicine and Surgery will hold its next meeting at the Kitchi Gammi Club in Duluth, Friday evening, August 27, 1954. Dinner will be at 7:00 p.m. preceded by a social hour.

The scientific session will include a discussion of "Hand Injuries" by Dr. John C. Feuling of Duluth and a description of "The Taconite Research and Development in Minnesota" by Mr. Edward Schmid, Public Relations Chief for the Reserve Mining Company. The participants have been invited by the Reserve Mining Company to tour its plant, particularly the Health Service, on Saturday morning.

## REPORTS AND ANNOUNCEMENTS

### SOUTHERN MINNESOTA MEDICAL ASSOCIATION

The annual meeting of the Southern Minnesota Medical Association will be held this year at Winona as an all-day session on Monday, September 13. The tentative program is as follows:

#### Morning Session—9:00-12:00

"Carcinoma of the Common Duct." Report of two cases.  
WILLIAM A. FINKELNBURG, M.D., Winona.

"Indications and Contraindications for Tonsillectomy."  
J. D. SJODING, M.D., Mankato.

"The Problem of Massive Gastric Hemorrhage with Cause Unknown Pre-operatively." C. E. REA, M.D., Saint Paul.

"Some Fundamental Considerations in Diagnosis and Treatment of Tumors of the Colon and Rectum."  
W. A. FANSLER, M.D., and WILLIAM T. SMITH, M.D., Minneapolis.

"Psychoses Associated with the Post-Partum Period."  
E. M. HAMMES, JR., M.D., Saint Paul.

"Current Status of Radio-isotopes in Diagnosis and Treatment of Blood Dyscrasias." C. F. STROEBEL, M.D., Rochester.

"Precautions in the Use of Cortisone." EMERSON WARD, M.D., Rochester.

"Hearing Loss in Children: Detection, Treatment, and Rehabilitation." K. M. SIMONTON, M.D., Rochester.

#### Afternoon Session—2:00-5:00

"Cardiac Surgery."  
(To be announced).

"Tumors of the Brain and Spinal Cord as They Concern the General Surgeon." H. J. SVIEN, M.D., Rochester.

"The Nursing Education Problem in Minnesota."  
Thelma Dodd, R.N., Saint Paul.

"Teratoma of the Pelvic Colon Presenting in the Lumen"—Case report. S. T. KUCERA, M.D., Northfield.

"Pulmonary Hypertension Due to Thrombo-Embolic Pulmonary Arterial Disease Following Pregnancy"—Case report. BEN SOMMERS, M.D., Saint Paul.

"Meconium Peritonitis"—Case report. G. R. MCNEAR, JR., M.D., Mankato.

"Case Report: Giant Condyloma (verruca) simulating Carcinoma of the Penis"—Case report. I. FISHER, M.D., Minneapolis.

"Lipoid Pneumonia: The Problems of Differential Diagnosis of Lung Shadows." J. GORDON BEATON, M.D., Northfield.

### AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

Applications for certification (American Board of Obstetrics and Gynecology) for the 1955 Part I Examinations are now being accepted. Candidates are urged

to make such application sometime in July or August.

All candidates for admission to the Examinations are required to submit with their application, a plain type-written list of all patients admitted to the hospitals where they practice, for the year preceding their application or the year prior to their request for reopening of their application, with the diagnosis, pathological diagnosis, nature of treatment, and end result.

Under a change of requirements for the Part I Examination, candidates must submit twenty case abstracts rather than twenty-five as formerly. Five of these may be from one's residency service.

Application for examination or re-examination, as well as requests for resubmission of case abstracts, must be made to the Secretary prior to October 1, 1954, and should be addressed as follows: Robert L. Faulkner, M.D., Secretary, 2105 Adelbert Road, Cleveland 6, Ohio.

### PEDIATRIC REUNION TO HONOR DOCTOR MCQUARRIE

In honor of twenty-five years of distinguished service to the University of Minnesota, Dr. Irvine McQuarrie, head of the department of pediatrics, will be honored at a pediatrics grand reunion September 23-25 at the University.

Colleagues and students of Dr. McQuarrie have planned the reunion in conjunction with the annual Northwestern Pediatric Society meeting.

Lectures will be delivered at the meeting by twenty-two academic leaders in the field of pediatrics. Most of them received their pediatric training under Dr. McQuarrie.

As an additional tribute to the University pediatric chief, a McQuarrie Pediatrics Fund has been established with a goal of \$50,000. An annual source of income from it will be earmarked: to provide a lectureship in pediatrics, as a scientific travel fund for pediatrics staff members to attend special conferences, to provide fellowships in unusual circumstances, to provide necessary equipment that may be needed from time to time by the department and for any other purpose within the department as approved by the committee.

Dr. McQuarrie, a graduate of the University of Utah who received his doctor of philosophy degree from the University of California and his doctor of medicine degree from Johns Hopkins university, joined the University of Minnesota staff in 1929.

Before coming to Minnesota, he had served on staffs of the University of California, Henry Ford Hospital, Yale University and the University of Rochester. And in addition to his duties at the University during the past twenty-five years he was visiting professor of pediatrics at Peking Union Medical college in China and served on the China Medical Board of Rockefeller Foundation.

Lecturing assignments on pediatrics have taken him to the far corners of the world, including Japan, Brazil, Uruguay, Argentina, Chile, Peru, Canada, Mexico, Italy, Cuba and China.

Dr. McQuarrie is editor-in-chief of *Brennemann-*

MINNESOTA MEDICINE

## WOMAN'S AUXILIARY

McQuarrie System Practice in Pediatrics and is an associate editor of ten medical publications.

In addition to his personal contributions to the field of pediatrics, men trained by him are now spreading his educational theories on pediatrics in such places as the Universities of Texas, Louisiana, California, Iowa, Utah, Colorado and Oregon as well as Tulane University, Meharry College, Stanford University and Peking Union Medical College.

### CONTINUATION COURSES

The University of Minnesota will join the Minnesota Tuberculosis and Health Association in sponsoring a continuation course in *Tuberculosis Control for Lay Persons* October 11 to 13, 1954, at the Center for Continuation Study on the University Campus. Public health aspects of tuberculosis and other chest diseases will be stressed.

\* \* \*

A continuation course in *Dermatology for Specialists* will be held at the Center for Continuation Study October 28 to 30, 1954. The program will deal with many topics of current interest to practicing dermatologists; sarcoidosis will receive special emphasis. The program will be presented under the direction of Dr. Henry E. Michelson, Professor, Department of Medicine, and Director, Division of Dermatology, University of Minnesota.

\* \* \*

A continuation course in *Clinical Microscopy and Parasitology for Medical Technologists* will be held at the Center for Continuation Study November 15 to 17, 1954. Half of the three-day program will be devoted to the examination of various body fluids such as urine, spinal fluid, and gastric secretion; the remainder to parasitology. Guest faculty will include Dr. Donald B. McMullen, Chief, Department of Medical Zoology, Army Medical Service Graduate School, Washington, D.C.

### UROLOGY AWARD

The American Urological Association offers an annual award of \$1000 (first prize of \$500, second prize \$300 and third prize \$200) for essays on the result of some clinical or laboratory research in urology. Competition shall be limited to urologists who have been graduated not more than ten years, and to men in training to become urologists.

The first prize essay will appear on the program of the forthcoming meeting of the American Urological Association, to be held at the Biltmore Hotel, Los Angeles, California, May 16-19, 1955.

For full particulars, write the Executive Secretary, William P. Didusch, 1120 North Charles Street, Baltimore, Maryland. Essays must be in his hands before January 1, 1955.

## Woman's Auxiliary

### DATE CHOSEN FOR AUXILIARY PROGRAM

October 1 is the date set for the annual School of Instruction of the Woman's Auxiliary of the Minnesota State Medical Association, according to Mrs. Peter S. Rude of Duluth, president of the organization.

The day's events will begin with registration and a Board meeting at 9 a.m., to be followed by a series of talks and panel discussions plus a luncheon and a special luncheon program. The place is the Hotel Radisson in Minneapolis, and Auxiliary members from all over the state will be invited to attend.

Several nationally known speakers are expected to take part in the program, including the new president of the Woman's Auxiliary to the American Medical Association, Mrs. George Turner of El Paso, Texas.

### RAMSEY COUNTY REPORTS ACTIVITIES

Current activities of the Woman's Auxiliary to the Ramsey County Medical Society are chiefly directed toward raising funds for local and national projects of interest to doctors' wives, according to Mrs. L. T. Simons, chairman for MINNESOTA MEDICINE.

Neighborhood House and the Hallie Q. Brown Neighborhood House benefited chiefly by 1953-54 fund-raising activities with Mrs. Philip K. Arzt, president of the Auxiliary, in charge. The purpose was to help send children to summer camps. A gift was also sent during this period for use of the University of Minnesota to the American Medical Association Research and Scholarship Fund.

Mrs. W. P. Gardner, who was elected to succeed Mrs. Arzt for 1955, called a meeting of the Auxiliary Board at her home, June 21, to plan other fund-raising activities to benefit the American Medical Education Fund. A "Kick-Off Fall Fashion Show and Luncheon" is the first event planned for this purpose. It will be held September 23 at the Saint Paul Hotel with Mrs. M. Dudley Hilker as general chairman and Mrs. W. A. Carley as co-chairman. Other committee chairmen appointed at the meeting are: Mrs. Rodney F. Sturley and Mrs. C. T. Eginton, tickets; Mrs. Duane R. Ausman, hostesses; Mrs. Douglas R. Kusske, decorations and Mrs. G. E. Knutson, door prizes.

An exhibit showing work of the Auxiliary and presented in connection with the Middle States Public Health meeting, June 4, at the Saint Paul Hotel, was also arranged and manned by the Ramsey county group with Mrs. R. K. Grau in charge.

## ♦ Of General Interest ♦

**Dr. John J. Hochfilzer**, Saint Paul, will deliver a lecture on "Endotracheal Anesthesia in Children" before the Austrian Otolaryngological Society in Bregenz, Austria, September 11, 1954. Dr. and Mrs. Hochfilzer left for Austria by plane on August 10.

\* \* \*

**Dr. Henry W. Goehrs**, Saint Cloud, was elected President of the Great Northern Railway Surgeons' Association at its annual meeting in Great Falls, Montana, June 29, 1954. Dr. Goehrs presented a paper on "The Silicosis Problem" with a number of films taken over a period of several years.

\* \* \*

**Dr. William C. Bernstein**, Saint Paul, has been promoted to Clinical Associate Professor of Surgery and Proctology, according to an announcement by the Board of Regents of the University of Minnesota following their June meeting. Dr. Bernstein has been active in the teaching programs at the University Hospitals, U. S. Veterans Hospital and Ancker Hospital.

\* \* \*

**Dr. Gordon R. Kamman**, Saint Paul, was Moderator at a round-table discussion at the Center for Continuation Study, University of Minnesota, on the subject "Continuation Course in New Developments in Nursing Home Care." On the panel were Dr. Jeanette Baker, Mr. Stuart Atkinson and Mrs. Mary Swanson, all of Fergus Falls. Dr. Baker is the Medical Director of the Geriatric Program at the Fergus Falls State Hospital; Mr. Atkinson is the Clinical Psychologist in charge of this project and Mrs. Swanson is the Chief Social Service Worker at Fergus Falls. More than 150 people attended the meeting.

\* \* \*

**Dr. Edward C. Maeder**, Minneapolis, announces the association of Dr. William E. Taylor of Saint Paul in the practice of obstetrics and gynecology at 1051 Medical Arts Building, Minneapolis. Dr. Taylor has just completed a two-year residency in obstetrics and gynecology at St. Mary's Hospital, Minneapolis.

\* \* \*

**Dr. David D. Norman**, who has just completed his postgraduate Fellowship in Neurology and Psychiatry at the Medical School of the University of Minnesota and the Veterans Hospital, Minneapolis, has become associated in the practice of neurology and psychiatry with Doctors Hammes and Hammes at 1124 Lowry Medical Arts Building, Saint Paul.

\* \* \*

**Dr. Harold Basinger**, after a year of study under a fellowship at Williamsport Hospital, Williamsport, Pennsylvania, has returned to Windom to be associated in practice with his father, Dr. Homer

Basinger, and with Dr. Harvey Basinger and Dr. Elmer Schutz of Mountain Lake. Dr. Basinger holds the rank of Lieutenant (jg) in the Navy.

\* \* \*

**Dr. F. W. Behmler**, Morris, has filed as a candidate for the State Senate from the 48th District, which comprises the counties of Stevens, Traverse, Big Stone and Grant. Dr. Behmler will seek the office now held by Senator A. R. Johanson of Wheaton, who has announced that he will not be a candidate for re-election this year. Dr. Behmler, who is first vice president of the Minnesota State Medical Association and is serving his second year as president of the Minnesota State Board of Health, was among the first to be mentioned as a possible candidate from his district, after Senator Johanson's announcement. He has practiced medicine in Morris for the past eighteen years.

\* \* \*

Sympathy is extended to **Dr. and Mrs. Lawrence R. Boies**, of Hopkins, in the loss of their son, William M. Boies, a student at the University of Wisconsin, who was accidentally drowned while picnicking with a group on the Baraboo Bluffs near Sauk City, Sunday, July 11, 1954.

\* \* \*

**Dr. and Mrs. N. W. Barker**, of Rochester, have returned from a trip to Europe, where Dr. Barker attended the International Congress on Thrombosis and Embolism in Basle, Switzerland. Dr. and Mrs. Barker enjoyed a six weeks' tour including Paris, Geneva, Lucerne, Basle, Innsbruck, Salzburg, Heidelberg, Cologne, Amsterdam, London and rural southern England. Included was a trip down the Rhine River by boat.

\* \* \*

**Dr. J. S. Blumenthal**, of Minneapolis, has been promoted to Associate Professor of Internal Medicine and Allergy at the University of Minnesota and was made chief of the Allergy Clinic.

\* \* \*

**Dr. J. A. Cosgriff, Sr.**, of Olivia, was elected first vice president of the Minnesota Heart Association at the annual meeting held in July. Dr. Cosgriff served as a member of the Board of Directors the past year.

\* \* \*

**Dr. James S. Cole**, who recently completed a residency at Ancker Hospital, has become associated with the Oxboro Clinic, Minneapolis, and will confine his practice to internal medicine. Dr. Cole is a graduate of Indiana University School of Medicine, 1947.

\* \* \*

**Dr. Eleanor Colle**, of Minneapolis, and **Dr. Lloyd D. MacLean**, of Calgary, Alberta, Canada, were united in marriage at St. John's Episcopal Church,

## OF GENERAL INTEREST

Linden Hills, June 30, 1954. The bride is a staff member of the pediatrics department of the University Hospitals; the groom is serving his residency in surgery at University Hospitals, having received his M. D. degree from the University of Alberta. Dr. and Mrs. MacLean are now at home at 132 Orlin Avenue S.E., Minneapolis.

\* \* \*

**Dr. Lorin D. Dawson**, who recently completed a surgery residency at Veterans Hospital, Minneapolis, has been appointed staff surgeon of the Worthington Clinic, Worthington. Dr. Dawson is a graduate of the University of Wisconsin Medical School and interned at the University of Pennsylvania before. He practiced for a time in Milbank, South Dakota, before coming to the Twin Cities for special training in surgery.

\* \* \*

**Dr. and Mrs. E. C. Elkins**, of Rochester, have returned from a two months' sojourn in Europe, where Dr. Elkins attended the meeting of the International Federation of Physical Medicine in Ostend, Belgium. While traveling in Europe, Dr. Elkins visited medical centers in Rotterdam, London, Stockholm, Copenhagen and Zurich. He and Mrs. Elkins toured England, Scotland, The Netherlands, Italy, France and Belgium.

\* \* \*

**Dr. George B. Eusterman**, of Rochester, has returned to his home there after spending eighteen months in Detroit, Michigan, helping to organize the medical department of the new Sinai Hospital there. He served as chief of the medical staff and director of Medical Education and was instrumental in having the hospital accrediting for intern and resident training. At present, Dr. Eusterman is completing a history of the department of medicine of the Mayo Clinic for the Clinic archives.

\* \* \*

**Dr. and Mrs. T. R. Fritzsche**, of New Ulm, have returned from Ulm, Germany, where Dr. Fritzsche, as Mayor of New Ulm, acted as official delegate from his home town at the 1100th birthday celebration of the ancient city for which New Ulm was named. During Dr. Fritzsche's absence, Dr. R. O. Leavenworth, Jr., of Saint Paul, took care of his practice which is devoted to diseases of the eye, ear, nose and throat.

\* \* \*

**Dr. Darwin K. Holian**, who has been a fellow at Minneapolis General Hospital since 1951, has been named to fill a newly created post with the Medical and Surgical Center in Albert Lea. He will limit his practice to general surgery and orthopedics. Dr. Holian, a native of Maynard, Minnesota, is a graduate of the University of Minnesota School of Medicine and served in the U. S. Army Medical Corps for two years.

\* \* \*

**Dr. Stuart W. Harrington**, head of the section of surgery in the Mayo Clinic since 1920 and professor

of surgery in the Mayo Foundation since 1936, retired from Clinic practice in July. Dr. Harrington was honored by his assistants who came from all parts of the country to participate in a dinner party at which they presented the honor guest with a silver tray engraved with their names.

\* \* \*

**Dr. William H. Henney**, of McIntosh, was guest of honor on "Dr. Henney Appreciation Day," June 19, 1954, when his townsmen gathered to pay their respects to the physician who has served them as physician and mentor for the past forty-six years.

\* \* \*

**Dr. Arthur J. Myers**, Minneapolis, received the honorary degree of Doctor of Laws at Ohio University on June 13, 1954.

\* \* \*

**Dr. E. J. Engberg**, Faribault, was among those certified as a competent mental hospital administrator by the Committee on Certification of Mental Hospital Administrators of the American Psychiatric Association at the meeting held in St. Louis in May.

\* \* \*

**Dr. J. V. Wallinga**, who has been practicing child psychiatry in Minneapolis and serving as psychiatric consultant to the Child Services Division, State Department of Public Welfare, has been recalled into the Navy. He will report to Oakland Naval Hospital, Oakland, California. Dr. Wallinga received certification by the American Board of Psychiatry and Neurology in May, 1954.

\* \* \*

**Dr. Paul Hedenstrom**, son of the late Dr. L. H. Hedenstrom, has joined the staff of the Cambridge Clinic. Dr. Hedenstrom received his medical degree from the University of Minnesota and interned at a Duluth hospital.

\* \* \*

**Dr. E. H. Haberman**, Osakis, was the recipient of an ovation in June when members of the Osakis community gathered to pay tribute to his long years of service to the Osakis residents and to commemorate the golden anniversary of his graduation from medical school. Dr. Haberman was presented with a gold medal in honor of the event.

\* \* \*

**Dr. and Mrs. Edward N. Peterson**, Virginia, attended the University of Minnesota commencement exercises June 12, when two of their sons received degrees from the University of Minnesota School of Medicine. Edward, who received the degree of doctor of medicine, is now in Buffalo, New York, where he will intern at the Edward J. Meyer Memorial Hospital. Charles, who received the bachelor of arts degree, cum laude, will be a sophomore in medical school next year.

\* \* \*

**Dr. S. A. Slater**, Worthington, recently attended the meeting of the National Tuberculosis Association at Atlantic City, New Jersey, where he was re-elected to the Board of Directors. He has served on the

## OF GENERAL INTEREST

board for twenty-four years, longer than any other member. He also attended the forty-fifth reunion of his medical school class at the Medical College of Virginia.

\* \* \*

**Dr. F. W. Behmler**, Morris, attended a meeting of the State Board of Health in Minneapolis on June 1. He also attended the Middle States Public Health conference in Saint Paul, June 2, and presented the welcoming address to the visiting public health officials from a number of states.

\* \* \*

**Dr. and Mrs. D. R. Navratil**, Montgomery, are now in Baltimore, Maryland, where the doctor is taking a three-year postgraduate course in surgery at Johns Hopkins University and the University of Maryland Medical School.

\* \* \*

**Dr. Karl R. Lundberg**, former Army specialist in preventive medicine, took over his duties as Minneapolis commissioner of health on June 15.

\* \* \*

**Dr. Louis J. Wilson**, who has just completed a tour of military service in the Navy Medical Corps, has returned to Winona and is resuming practice with his father, **Dr. R. H. Wilson**.

\* \* \*

United States Public Health Service fellowships have been awarded to two residents in surgery at Ancker Hospital, Saint Paul, Dr. Joseph L. Sprafka, Jr., was named a "national heart trainee" and Dr. Truman J. Newberry, "a national cancer trainee."

\* \* \*

**Dr. Howard K. Gray**, Mayo Clinic surgeon, was awarded the honorary degree of Doctor of Science by the University of Nebraska College of Medicine in Omaha, at the June graduation exercises.

\* \* \*

**Dr. T. C. Chisholm**, Minneapolis, spoke to the Range Medical Association on June 22 at the Itasca Memorial Hospital. His topic was "Latest Developments in the Field of Children's Surgery."

\* \* \*

**Dr. and Mrs. H. W. Meyerding**, Rochester, recently returned from a two-month vacation in South America. While in Sao Paulo, Dr. Meyerding spoke before the International Surgical Society.

\* \* \*

**Dr. Gilman Goehrs**, St. Cloud, was recently re-elected state surgeon of the Veterans of Foreign Wars at the encampment of the service organization at Hibbing.

\* \* \*

**Dr. Donald W. Mulder** has returned to the Mayo Clinic after fourteen months of active duty in the Navy in the Pacific theater. Dr. Mulder, who is a consultant in the section of neurology and psychiatry, held the rank of lieutenant commander. He was recalled into service in March, 1953, to carry out a study of head injuries incident to the Korean war.

After the cease fire, he took part in a study of amyotrophic lateral sclerosis, an assignment that took him to Guam and other South Pacific islands.

\* \* \*

**Dr. Viktor O. Wilson**, Rochester, has been renamed city-county health officer of Rochester and Olmsted County.

\* \* \*

A new children's clinic has opened in Wayzata. Three pediatricians, **Dr. E. J. Huennekens**, **Dr. R. D. Semsch** and **Dr. D. H. Petersen** make up the staff of the clinic.

\* \* \*

**Dr. John Carroll**, Winsted's new physician, has joined the staff of the Glencoe Hospital.

\* \* \*

Twenty-one Minnesota doctors, celebrating their fifty years in the practice of medicine were honored by the State Medical association at its annual banquet in Duluth, June 8. Those so honored were: **Drs. Albert E. Ahrens**, Saint Paul; **Jacob Biedermann**, Thief River Falls; **William A. Brand**, Redwood Falls; **Hermanus DeBoer**, Edgerton; **Herbert Z. Giffin**, Rochester; **Emil Haberman**, Osakis; **John G. W. Havens**, Austin; **Andrew D. Hoidale**, Tracy; **LeRoy J. Holmberg**, Canby; **Alva E. Holmes**, Rush City; **John E. Hymes**, Minneapolis; **Claude B. Lewis**, St. Cloud; **George R. Melzer**, Lyle; **R. P. Pearsall**, Virginia; **Joseph W. Preisinger**, Dallas, Texas; **Albert G. Schulze**, Saint Paul; **Ivar Sivertsen**, Minneapolis; **George E. Thomas**, Minneapolis; **Leon A. Williams**, Minneapolis; **Rasmus V. Williams**, Rushford; **Andrew Gullixson**, Longmont, Colorado.

\* \* \*

**Dr. Frederick A. Figi**, head of the section of oral and plastic surgery, Mayo Clinic, received an honorary Doctor of Science degree from the University of Nebraska, at the 83rd commencement exercises in June. He was also one of the speakers at the American Medical association meeting in San Francisco, June 21-25.

\* \* \*

The Damon Runyon Memorial fund has awarded \$15,000 to the University of Minnesota to permit **Dr. Owen H. Wangensteen**, chief of the university's surgery department, to continue with his "second look" project for patients with gastric, colic or rectal cancer.

\* \* \*

**Dr. M. W. Comfort**, Mayo Clinic staff member and professor of medicine in the Mayo foundation graduate school since 1946, was awarded the honorary degree of Doctor of Laws by Austin College, Sherman, Texas, at the commencement exercises in June.

\* \* \*

**Dr. Howard O. Mortenson** of Menahga and Miss Carol Jean Jarvinen, also of Menahga, were united in marriage June 21, 1954. Dr. and Mrs. Mortenson are now at home in Menahga following a trip to Banff and Lake Louise, Canada.

## OF GENERAL INTEREST

**Dr. Charles P. Robbins** of Winona this year completed fifty-nine years of practice in Winona, where he came a year following his graduation from Jefferson Medical College in 1894. Although Dr. Robbins discontinued office practice about three years ago, owing to a back injury, he still maintains an office at his residence.

### NEW LOCATIONS

**Dr. Kristofer Hagen**, formerly of Cokato, is now located in Richfield.

**Dr. Henry B. Blumberg**, Fairmont physician, has accepted a position as chief resident of the San Joaquin County Hospital in Stockton, California, where he will head a staff of twelve doctors. He intends to obtain further specialized training in internal medicine for one year and then return to Fairmont.

**Dr. E. Duane Sommerness** is the new clinical director at the Fergus Falls State Hospital. Dr. Sommerness formerly was clinical director at the Willmar Hospital.

**Dr. Leighton W. Larson**, formerly associated with Dr. J. W. Bretholdt at Watertown, is now engaged in practice at Waconia.

**Dr. Joseph W. Burnett**, formerly of Fergus Falls, is the new consultant at Union Hospital and Loretta Hospital in New Ulm, and at the Sleepy Eye Hospital.

**Dr. Philip J. Parker**, who has been associated with the Bratrud Clinic in Thief River Falls for the past three years, has opened an office in Hallock.

**Dr. Ernest Ager** is now located in Le Center. He formerly practiced in Minneapolis.

**Dr. Carl O. Bretzke** has moved from Greenbush to Hutchinson, where he has opened an office for the practice of medicine.

**Dr. John Bouma**, who has been associated in practice with Dr. Gerrit Beckering at Edgerton, has been awarded a three-year fellowship in psychiatry at the Menninger Foundation in Topeka, Kansas. Dr. Bouma started his work under the fellowship July 1.

**Dr. William Alden**, at present a lieutenant colonel in the Air Force, plans to open a medical practice in Kimball, upon his release from the Air Force.

**Drs. M. J. Bernier and R. W. Reif** of Saint Paul are now located in their new offices at 721 Margaret Street.

**Dr. Calvin Elrod**, who has been associated in practice with Dr. William I. Davis at Mound the past two years, has moved with his wife and two children to Long Lake, where he started his practice in July.

**Dr. Bradley W. Kusske**, who was associated with Dr. D. Howard Vogel in the Vogel Clinic at New Ulm for three years, is now practicing medicine in Saint Paul with Dr. A. W. Hilger, Dr. Jerome A. Hilger, and his brother, Dr. Douglas R. Kusske.

**Dr. E. R. Crow** has left Walker, where he maintained an office with Dr. O. F. Ringle, to take a position with the Healthwin Hospital for tuberculosis patients at South Bend, Indiana.

### MINNESOTA BLUE SHIELD-BLUE CROSS

During the recent annual meeting of the Minnesota State Medical Association in Duluth, many doctors and their office personnel visited the Blue Cross and Blue Shield booth. Compared with previous years, the number of visitors at the booth and the interest in Blue Shield matters made it a banner year. Not only were practicing physicians and their office nurses, receptionists and secretaries among the callers, but also doctors in residencies, internships and advanced study visited the booth.

In order to provide any requested information to members of the medical profession and other interested visitors, representatives of the Blue Cross-Blue Shield staff were constantly on hand. Interest of the physicians embraced a wide range of subjects such as enrollment, the different services covered by the contract, comparison of Plan A and Plan B contracts and fees, and identification of Plan A and Plan B subscribers. Discussion with the members of the doctors' offices primarily involved matters relating to the filing and payment of claims.

The fact that a representative of Blue Shield was in attendance at the booth furnished an excellent opportunity for the exchange of suggestions and information between the Blue Shield representatives and the visiting doctors. Many of the questions disclosed a need for a more intensive professional relations program directed toward keeping the profession informed about Blue Shield matters and assisting the personnel of doctors' offices in promptly and properly filing claims. Many recent graduates, interns and resident physicians were most interested in how to become a participating Blue Shield physician.

Another feature attracting attention was the Blue Shield plaque for display in the doctor's office. This plaque consists of a Blue Shield with a central gray caduceus placed upon a gray background. On the face are printed the words, "Participating Doctor of Medicine, Minnesota Medical Service, Inc." These plaques are useful in encouraging the patients to show their Blue Shield identification cards so that claims may be filed early and payment made promptly. Any participating physician who wishes to have a Blue Shield plaque may obtain one by writing Minnesota Medical Service, Inc., 2610 University Avenue, Saint Paul 14, Minnesota.

During the month of May, 4,624 contracts representing 10,649 participant subscribers were enrolled in Blue Cross, bringing the net enrollment as of May 31, 1954 to a total of 378,019 Blue Cross contracts covering 1,003,140 participant subscribers.

Enrollment in Blue Shield during the month of May, 1954, was increased by 1,423 contracts representing 9,029 participant subscribers bringing the net enrollment as of May 31, 1954, to 241,798 Blue Shield contracts covering 635,130 participant subscribers. As of May 31, 1954, there were 240,762 Plan A contracts in effect covering 633,424 participant subscribers and 1,036 Plan B contracts covering 1,706 participant subscribers.

## BOOK REVIEWS

### BOOK REVIEWS

Books listed here become the property of the Ramsey, Hennepin and St. Louis County Medical Libraries when reviewed. Members, however, are urged to write reviews of any or every recent book which may be of interest to physicians.

### BOOKS RECEIVED FOR REVIEW

**ILLUSTRATED REVIEW OF FRACTURE TREATMENT.** Frederick Lee Liebolt, A.B., M.D., Sc.D., LL.D. Attending Surgeon in Charge of Orthopedics, New York Hospital; Attending Orthopedic Surgeon, Hospital for Special Surgery; Associate Professor of Clinical Surgery (Orthopedics), Cornell University Medical College, 1954.

**PRIMER OF ALLERGY.** Warren T. Vaughan, M.S., M.D., Richmond, Virginia. Fourth Edition, Revised by J. Harvey Black, M.D., Dallas, Texas. 191 pages. Illus. Price \$4.25, cloth. St. Louis: C. V. Mosby Co., 1954.

**THE PHYSICIAN AND HIS PRACTICE.** By Eighteen Authorities. Edited by Joseph Garland, M.D., editor of The New England Journal of Medicine. 270 pages. Price \$5.00, cloth. Boston: Little, Brown & Co., 1954.

**ANNUAL REPORT ON THE RESULTS OF TREATMENT IN CARCINOMA OF THE UTERUS.** J. Hayman, M.D., Editor, and Committee. 256 pages. Illus. Paper cover. Stockholm, Sweden: Radiumhemmet, 1954.

**BCG AND VOLE VACCINATION.** A practical handbook. By K. Neville Irvine, MA, DM, BCh, MRCS, LRCP, Adviser in BCG Vaccination to Oxford Regional Hospital Board. 96 pages. Illus. 10 colored plates. Price 12s. 6d. London: The National Association for the Prevention of Tuberculosis, 1954.

This pocket-size book contains a comprehensive index, a number of black and white illustrations and ten colored plates. It gives a concise summary of what is known about the BCG and vole vaccines, and outlines the theory of vaccination. Practical instructions for tuberculin testing by a variety of methods are followed by instructions on the technique of intracutaneous vaccination, the multiple-puncture method, scarification and oral vaccination. Further chapters deal with the complications of vaccination and the organization of vaccination procedure.

The four pages of colored plates illustrate clearly the results obtained by a positive tuberculin test, using four different methods, and show the results of intracutaneous BCG vaccination (in four progressive stages) and of multiple-puncture vaccination.

In a Foreword, Frederick Heaf, MA, MD, FRCP, David Davies Professor of Tuberculosis, The Welsh National School of Medicine, says, "There can be no doubt that this small book on a complicated and intricate subject will, by its clarity and lucidity, help many who are already using the vaccines. It will help many more who are as yet only vaguely acquainted with the subject to understand and take a greater interest in this work of national importance."

### ACUTE PERFORATED PEPTIC ULCER

(Continued from Page 611)

3. Inability to completely empty the stomach for any reason should be considered a contraindication to the non-operative regime. We have not considered a recent meal as an absolute contraindication to this method of treatment, although the initial emptying of the stomach is more difficult and time-consuming.

4. Theoretically, a huge perforation, such as those occasionally seen from a large carcinomatous ulcer on the anterior aspect of the stomach, might not respond to non-operative treatment. However, benign peptic ulcer perforations of apparently quite large size were treated non-operatively by us with no unusual difficulties.

### Conclusions

We feel that the non-operative management of acute perforated peptic ulcer, if properly conducted, is a safe and effectual means of handling this acute abdominal catastrophe. The non-operative regime has many advantages over the operative treatment in that the complications of the operation itself, few as these may be, are avoided, and the recovery period is easier and shorter. There are definite contraindications to the use of this method of treatment. There are also very definite hazards which can be avoided only by strict adherence to rigid rules of management.

\* \* \*

Dr. Ray Hedin, of Red Wing, Minnesota, then read his inaugural thesis on "Parotid Tumors." Lantern slides were shown. (Published in June, 1954, issue.)

The meeting was adjourned.

ROBERT E. PRIEST, M.D., Secretary

### TRUDEAU SANATORIUM PAMPHLET AVAILABLE

A new twenty-page illustrated folder on Trudeau Sanatorium has just been issued by that Institution.

Printed in two colors, the pamphlet describes the facilities of Trudeau and is designed primarily to give prospective patients general information about the Sanatorium. Copies were mailed in mid-May to 14,500 physicians east of the Mississippi.

Additional copies are available from Dr. Roger S. Mitchell, Clinical Director, Trudeau Sanatorium, Trudeau, New York.

### NEW EXHIBIT ON SINUS TROUBLE

Persons suffering from clogged heads or draining noses will be especially interested in the new exhibit—"Sinus Trouble"—which the AMA Bureau of Exhibits now is offering to state and county medical societies for local showings at fairs and similar public gatherings. Depicting the location of the sinuses, diagnostic procedures and latest treatments now followed by physicians, this exhibit is available for immediate bookings through the Bureau.